

## DESCRIPTION

AMIDE COMPOUNDS AND METHOD FOR CONTROLLING PLANT DISEASES WITH  
THE SAME

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Technical Field

The present invention relates amide compounds and a method for controlling plant diseases applying the same for plants or soils growing the plant.

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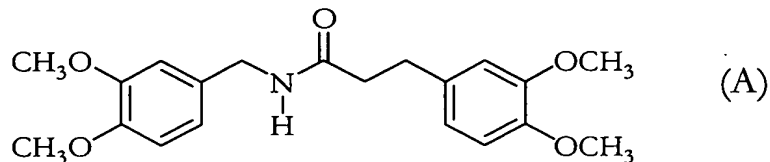
Background Art

The development of plant diseases controlling composition have been carried out, and many compounds which have a controlling activity against plant diseases was found out. However, sometimes their controlling activity are not always enough, and there have been studying to find out new compounds.

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On the other hand, though the amide compound (A) shown by the following formula is disclosed in Journal of Chemical Society, Perkin Transactions I, 6, p.661 (1976), the concrete use of said compound is not disclosed in it.

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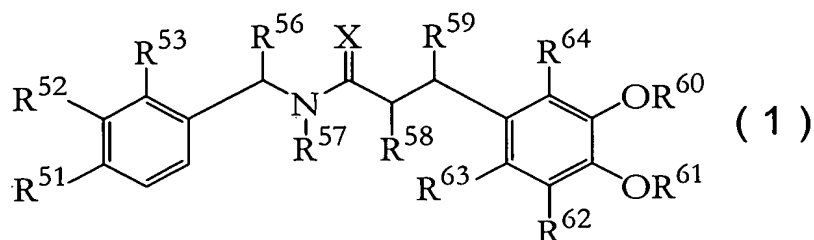
Disclosure of Invention

The present inventors, after intensively studying to find out the compounds which have an excellent controlling activity against plant diseases, have found that an amide compound shown

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by the following formula (1) has an excellent controlling activity against plant diseases and accomplished the present invention.

Namely, the present invention provides an amide compound (1) represented below (referred as "the compound of the present invention" hereinafter.):



wherein, in the formula,

$R^{51}$  represents a halogen atom, a C1-C6 alkyl group, a C3-C6 cycloalkyl group, a C1-C6 haloalkyl group, a C2-C6 alkenyl group, a C2-C6 haloalkenyl group, a C2-C6 alkynyl group, a C2-C6 haloalkynyl group, a C1-C6 alkoxy group, a C3-C6 alkenyloxy group, a C3-C6 alkynyloxy group, a C1-C6 haloalkoxy group, a (C1-C6 alkoxy)C1-C6 alkyl group, a phenoxy C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, a (C1-C6 alkyl sulfonyloxy) C1-C6 alkyl group, a C1-C6 alkylthio group, a C1-C6 haloalkylthio group, a C1-C6 alkylamino group, a di(C1-C6 alkyl)amino group, a formyl group, a (C1-C6 alkyl) carbonyl group, a (C1-C6 alkoxy) carbonyl group, a (C1-C6 alkoxy) imino C1-C6 alkyl group, benzyloxyimino C1-C6 alkyl group, a di(C1-C6 alkylamino) imino C1-C6 alkyl group, a tri(C1-C6 alkyl) silyl group, a phenyl group, a phenoxy group, a cyano group or a nitro group;  $R^{52}$  represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group, a C1-C6 haloalkyl group, a C2-C6 alkenyl group, a C2-C6 alkynyl group, a cyano group or a nitro group; or both of  $R^{51}$  and  $R^{52}$  are combined together to represent a C3-C6 alkylene group or a group of  $-CR^{65}=CR^{66}-CR^{67}=CR^{68}-$

(R<sup>65</sup>, R<sup>66</sup>, R<sup>67</sup> and R<sup>68</sup> independently represent a hydrogen atom, a halogen atom, a C1-C3 alkyl group, a C1-C3 alkoxy group or a C1-C3 haloalkyl group);

5 R<sup>53</sup> represents a hydrogen atom, a halogen atom, a C1-C3 alkyl group or a C1-C3 haloalkyl group;

R<sup>56</sup> represents a hydrogen atom, a C1-C4 alkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group;

R<sup>57</sup> represents a hydrogen atom, a C1-C4 alkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group;

10 R<sup>58</sup> and R<sup>59</sup> independently represent a hydrogen atom, a halogen atom or a C1-C3 alkyl group;

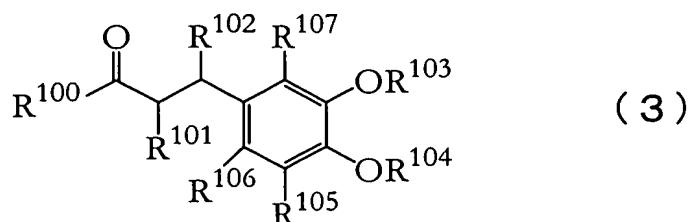
R<sup>60</sup> represents a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C6 alkynyl group;

15 R<sup>61</sup> represents a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C6 alkynyl group or a C2-C4 cyanoalkyl group;

each of R<sup>62</sup>, R<sup>63</sup> and R<sup>64</sup> represents a hydrogen atom, a halogen atom or a C1-C2 alkyl group;

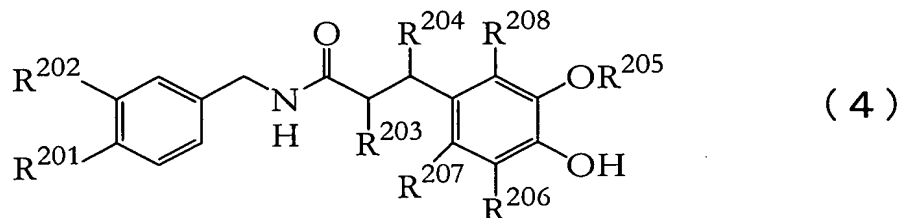
X represents an oxygen atom or a sulfur atom;

20 a plant diseases controlling composition comprising the compound of the present invention as an active ingredient; and  
a method for controlling plant diseases comprising a step applying an effective amount of the compound of the present invention to plants or soils growing the plant. The present invention also  
25 provides the compound (3) represented below (referred as "the intermediate 1 of the present invention" hereinafter.):



wherein, in the formula,

$R^{100}$  represents a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butyloxy group, an isopropoxyloxy group, a tert-butyloxy group, an OH group or a chlorine atom;  $R^{101}$  and  $R^{102}$  independently represent a hydrogen atom, a halogen atom or a C1-C3 alkyl group;  $R^{103}$  represents a C1-C4 alkyl group;  $R^{104}$  represents a C3-C6 alkynyl group;  $R^{105}$ ,  $R^{106}$  and  $R^{107}$  independently represent a hydrogen atom, a halogen atom or a C1-C2 alkyl group; and the amide compound (4) represented below (referred as "the intermediate 2 of the present invention" hereinafter.):



wherein, in the formula,

$R^{201}$  represents a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a di(C1-C4alkyl)amino group or a cyano group;  $R^{202}$  represents a hydrogen atom, a halogen atom, a C1-C4 alkyl group or a C1-C4 haloalkyl group; or both of  $R^{201}$  and  $R^{202}$  are combined together to represent a C3-C5 alkylene group or a group of  $-CH=CH-CH=CH-$ ;  $R^{203}$  and  $R^{204}$  independently represent a hydrogen atom, a halogen atom or a C1-C3 alkyl group;  $R^{205}$  represents a C1-C4 alkyl group,  $R^{206}$ ,  $R^{207}$  and  $R^{208}$  independently represent a hydrogen atom, a halogen

atom or a C1-C2 alkyl group;  
which are important intermediates in production of the compound  
of the present invention.

5           The substituents in the amide compound (1), the compound  
(2), and the amide compound (4) of the present invention are  
concretely exemplified below.

          In the representation of  $R^{51}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
10 bromine atom, an iodine atom;  
the C1-C6 alkyl group includes a C1-C4 alkyl group such as a  
methyl group, an ethyl group, a propyl group, an isopropyl group,  
a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl  
group; a C5-C6 alkyl group such as a pentyl group, a 2-methylpentyl  
15 group, a 3-methylpentyl group, a 4-methylpentyl group, a hexyl  
group and the like;  
the C3-C6 cycloalkyl group includes a cyclopropyl group, a  
cyclobutyl group, a cyclopentyl group and a cyclohexyl group;  
the C1-C6 haloalkyl group includes, for example, a C1-C4 haloalkyl  
20 group such as a fluoromethyl group, a difluoromethyl group, a  
trifluoromethyl group;  
the C2-C6 alkenyl group includes, for example, a C2-C4 alkenyl  
group such as a vinyl group, a 1-methylvinyl group, a 1-propenyl  
group, a 2-propenyl group, a 1-methyl-2-propenyl group, a  
25 2-methyl-2-propenyl group, a 2-butenyl group, a 3-butenyl group  
and the like; a C5-C6 alkenyl group such as a 1-pentenyl group,  
a 4-pentenyl group, a 1-hexenyl group, a 5-hexenyl group and  
the like;

the C2-C6 haloalkenyl group includes, for example, a 2-fluorovinyl group, a 2-chlorovinyl group, a 2-bromovinyl group, a 2,2-difluorovinyl group, a 2,2-dichlorovinyl group, a 2,2-dibromovinyl group, a 1-methyl-2,2-dichlorovinyl group, a 1-methyl-2,2-dibromovinyl group;

the C2-C6 alkynyl group includes, for example, a C2-C4 alkynyl group such as an ethynyl group, a 1-propynyl group, a 2-propynyl group, 1-methyl-2-propynyl group, a 1-butynyl group, a 2-butynyl group, a 3-butynyl group and the like; a C5-C6 alkenyl group such as a 3,3-dimethyl-1-butynyl group, a 1-pentynyl group, a 4-pentynyl group, a 1-hexynyl group, a 5-hexynyl group and the like;

the C2-C6 haloalkynyl group includes, for example, a chloroethynyl group, a bromoethynyl group, a iodoethynyl group; the C1-C6 alkoxy group includes, for example, a C1-C4 alkoxy group such as a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group; a C5-C6 alkoxy group such as a pentyloxy group, a hexyloxy and the like;

the C3-C6 alkenyloxy group includes, for example, a 2-propenyloxy group, a 1-methyl-2-propenyloxy group, a 2-methyl-2-propenyloxy group, a 2-butenyloxy group, a 3-butenyloxy group, a 4-pentyloxy group, a 5-hexenyloxy group;

the C3-C6 alkynyloxy group includes, for example, a 2-propynyloxy group, a 1-methyl-2-propynyloxy group, a 2-butynyloxy group, a 3-butynyloxy group, a 3-pentyloxy group, a 4-pentyloxy group, a 5-hexynyloxy group;

the C1-C6 haloalkoxy group includes, for example, a C1-C4

haloalkoxy group such as a fluoromethoxy group, a difluoromethoxy group, a trifluoromethoxy group, a chloromethyl group, a dichloromethyl group, a trichloromethyl group, a 2,2,2-trifluoroethoxy group, a 1,1,2,2,-tetrafluoroethoxy group, a 2-fluoroethoxy group and the like;

the (C1-C6 alkoxy) C1-C6 alkyl group includes a methoxymethyl group, an ethoxymethyl group, a propyloxymethyl group, a 1-methoxyethyl group, a 2-methoxyethyl group, a 2-methoxypropyl group, a 2-methoxyisopropyl group;

the phenoxy C1-C6 alkyl group includes a phenoxy methyl group, a 1-phenoxyethyl group, a 2-phenoxyethyl group, a 1-phenoxypropyl group, a 3-phenoxypropyl group, a 4-phenoxybutyl group;

hydroxy C1-C6 alkyl group includes a hydroxymethyl group, a 1-hydroxyethyl group, a 2-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxybutyl group;

the (C1-C6 alkylsulfonyloxy) C1-C6 alkyl group includes a methylsulfonyloxymethyl group, a ethylsulfonyloxymethyl group, a 1-methylsulfonyloxyethyl group, a 2-sulfonyloxyethyl group, a 1-methylsulfonyloxypropyl group;

the C1-C6 alkylthio group includes, for example, a methylthio group, a ethylthio group, a propylthio group, a isopropylthio group, a butylthio group, a isobutylthio group, a sec-butylthio group, a tert-butylthio group, a pentylthio group, a hexylthio group;

the C1-C6 haloalkylthio group includes, for example, a fluoromethylthio group, a difluoromethylthio group, a trifluoromethylthio group;

the C1-C6 alkylamino group includes, for example, a C1-C4

alkylamino group such as a methylamino group, an ethylamino group, a propylamino group, an isopropylamino group; a pentylamino group, a hexylamino;

the di(C1-C6 alkyl)amino group includes, for example, a C1-C4 dialkylamino group such as a dimethylamino group, a diethylamino group, a dipropylamino group; a dipentylamino group, a dihexylamino group;

the (C1-C6 alkyl) carbonyl group includes a methylcarbonyl group, an ethylcarbonyl group, a propylcarbonyl group, an isopropylcarbonyl group;

the (C1-C6 alkoxy) carbonyl group includes a methoxycarbonyl group, a ethoxycarbonyl group, a propoxycarbonyl group, a isopropoxycarbonyl group;

the (C1-C6 alkoxyimino) C1-C6 alkyl group includes a methoxyiminomethyl group, a 1-methoxyiminoethyl group, a 1-methoxyiminopropyl group, a 1-methoxyiminobutyl group, an ethoxyiminomethyl group, a 1-ethoxyiminoethyl group, a propoxyiminomethyl group, a 1-isopropoxyiminoethyl group, a butoxyiminomethyl group, a pentyloxyiminomethyl group, a 1-hexyloxyiminoethyl group;

the benzyloxyimino C1-C6 alkyl group includes a benzyloxyiminomethyl group, a 1-(benzyloxyimino)ethyl group, a 2-(benzyloxyimino)ethyl group, a 1-(benzyloxyimino)propyl group, a 1-(benzyloxyimino)butyl group;

the di(C1-C6 alkyl)aminoimino C1-C6 alkyl group includes a dimethylaminoiminomethyl group, a 1-(dimethylaminoimino)ethyl group, a diethylaminoiminomethyl group, a 1-(diethylaminoimino)ethyl group;



the tri(C1-C6 alkyl) silyl group includes a trimethyl silyl group, a triethyl silyl group, a tert-butyldimethyl silyl group;

In the representation of  $R^{52}$ ,

the halogen atom includes a fluorine atom, a chlorine atom, a  
5 bromine atom, an iodine atom;

the C1-C6 alkyl group includes a C1-C4 alkyl group such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, sec-butyl group, tert-butyl group; a C5-C6 alkyl group such as a pentyl group, a 2-methylpentyl  
10 group, a 3-methylpentyl group, a 4-methylpentyl group, a hexyl group and the like;

the C1-C6 haloalkyl group includes, for example, a fluoromethyl group, a difluoromethyl group, a trifluoromethyl group;

the C2-C6 alkenyl group includes, for example, a C1-C4 alkenyl  
15 group such as a vinyl group, a 1-methylvinyl group, a 1-propenyl group, a 2-propenyl group, a 1-methyl-2-propenyl group, a 2-methyl-2-propenyl group, a 2-butenyl group, a 3-butenyl group and the like; a C5-C6 alkyl group such as a 1-pentenyl group, a 4-pentenyl group, a 1-hexenyl group, a 5-hexenyl group and  
20 the like;

the C2-C6 alkynyl group includes, for example, a C2-C4 alkynyl group such as an ethynyl group, a 1-propynyl group, a 2-propynyl group, a 1-methyl-2-propynyl group, a 1-butynyl group, a 2-butynyl group, a 3-butynyl group and the like; a C5-C6 alkynyl  
25 group such as a 1-pentynyl group, a 4-pentynyl group, a 1-hexynyl group, a 5-hexynyl group and the like;

the C3-C6 alkylene group represented by  $R^{51}$  and  $R^{52}$  are combined together includes, for example, a trimethylene group,

a tetraethylene group, a pentamethylene group and hexamethylene group.

In the representation of  $R^{53}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
5 bromine atom, an iodine atom;  
the C1-C3 alkyl group includes a methyl group, an ethyl group,  
a propyl group, an isopropyl group;  
the C1-C3 haloalkyl group includes, for example, a  
trifluoromethyl group.

10 In the representation of  $R^{56}$ ,  
the C1-C4 alkyl group includes a methyl group, an ethyl group,  
a propyl group, an isopropyl group, a butyl group, an isobutyl  
group, a sec-butyl group, a tert-butyl group;  
the C2-C4 alkenyl group includes, for example, a vinyl group,  
15 a 1-methylvinyl group, a 1-propenyl group, a 2-propenyl group,  
a 1-methyl-2-propenyl group, a 2-methyl-2-propenyl group, a  
2-butenyl group, a 3-butenyl group and the like;  
the C2-C4 alkynyl group includes, for example, an ethynyl group,  
a 1-propynyl group, a 2-propynyl group, a 1-methyl-2-propynyl  
20 group, a 2-butyne group, a 3-butyne group and the like.

In the representation of  $R^{57}$ ,  
the C1-C4 alkyl group, for example, includes a methyl group,  
an ethyl group, a propyl group, a butyl group;  
the C3-C4 alkenyl group includes, for example, a 2-propenyl group,  
25 a 1-methyl-2-propenyl group, a 2-methyl-2-propenyl group, a  
2-butenyl group, a 3-butenyl group and the like;  
the C3-C4 alkynyl group includes a 2-propynyl group,  
1-methyl-2-propynyl group, a 2-butyne group, a 3-butyne group

and the like.

In the representation of  $R^{58}$  and  $R^{59}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
bromine atom;

5 the C1-C3 alkyl group includes a methyl group, an ethyl group,  
a propyl group, an isopropyl group.

In the representation of  $R^{60}$ ,  
the C1-C4 alkyl group includes a C1-C2 alkyl group such as a  
methyl group, an ethyl group; a propyl group, an isopropyl group,  
10 a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl  
group;

the C1-C4 haloalkyl group includes, for example, a fluoromethyl  
group, a difluoromethyl group, a trifluoromethyl group, a  
2,2,2-trifluoroethyl group, a 1,1,2,2-tetrafluoroethyl group,  
15 a 2-fluoroethyl group;

the C3-C4 alkenyl group includes, for example, a 2-propenyl group,  
a 1-methyl-2-propenyl group, a 2-methyl-2-propenyl group, a  
2-butenyl group, 3-butenyl group;

the C3-C6 alkynyl group includes, for example, a C3-C4 alkynyl  
20 group such as 2-propynyl group, a 1-methyl-2-propynyl group,  
a 2-butyne group, a 3-butyne group and the like; a C5-C6 alkynyl  
group such as a 1,1-dimethyl-2-propynyl group, a  
1-methyl-2-butyne group, a 2-pentyne group, a  
1-methyl-2-pentyne group, a 4-methyl-2-pentyne group, a  
25 3-pentyne group, a 4-pentyne group, a 2-hexynyl group, a  
3-hexynyl group and the like;

In the representation of  $R^{61}$ ,  
the C1-C4 alkyl group includes a methyl group, an ethyl group,

a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group;

the C1-C4 haloalkyl group includes, for example, a fluoromethyl group, a difluoromethyl group, a trifluoromethyl group, a  
 5 2,2,2-trifluoroethyl group, a 1,1,2,2-tetrafluoroethyl group, a 2-fluoroethyl group;

the C3-C4 alkenyl group includes, for example, a 2-propenyl group, a 1-methyl-2-propenyl group, a 2-methyl-2-propenyl group, a 2-butenyl group, a 3-butenyl group;

10 the C3-C6 alkynyl group includes, for example, a C3-C4 alkynyl group such as a 2-propynyl group, a 1-methyl-2-propynyl group, a 2-butyne group, a 3-butyne group; a C5-C6 alkynyl group such as a 1,1-dimethyl-2-propynyl group, a 1-methyl-2-butyne group, a 2-pentyne group, a 1-methyl-2-pentyne group, a  
 15 4-methyl-2-pentyne group, a 3-pentyne group, a 4-pentyne group, a 2-hexynyl group, a 3-hexynyl group and the like;

the C2-C4 cyanoalkyl group includes, for example, a cyanomethyl group, a cyanoethyl group, a cyanopropyl group, a 1-methylcyanomethyl group, a 1,1-dimethylcyanomethyl group.

20 In the representation of  $R^{62}$ ,  $R^{63}$  and  $R^{64}$ , the halogen atom includes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom;

the C1-C2 alkyl group includes a methyl group and an ethyl group.

In the representation of  $R^{65}$ ,  $R^{66}$ ,  $R^{67}$  and  $R^{68}$ ,  
 25 the halogen atom includes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom;  
 the C1-C3 alkyl group includes a methyl group, an ethyl group, a propyl group, an isopropyl group;

the C1-C3 alkoxy group includes a methoxy group, an ethoxy group, a propyloxy group, an isopropyloxy group;

the C1-C3 haloalkyl group includes, for example, a trifluoromethyl group.

5           In the representation of  $R^{101}$  and  $R^{102}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a bromine atom;

the C1-C3 alkyl group includes a methyl group, an ethyl group, a propyl group, an isopropyl group.

10           In the representation of  $R^{103}$ ,  
the C1-C4 alkyl group includes a C1-C2 alkyl group such as a methyl group, an ethyl group; a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group.

15           In the representation of  $R^{104}$ ,  
the C3-C6 alkynyl group includes, for example, a C3-C4 alkynyl group such as a 2-propynyl group, a 1-methyl-2-propynyl group, a 2-butynyl group, a 3-butynyl group; a C5-C6 alkynyl group such as a 1,1-dimethyl-2-propynyl group, a 1-methyl-2-butynyl group,  
20   a 2-pentynyl group, a 1-methyl-2-pentynyl group, a 4-methyl-2-pentynyl group, a 3-pentynyl group, a 4-pentynyl group, a 2-hexynyl group, 3-hexynyl group.

          In the representation of  $R^{105}$ ,  $R^{106}$  and  $R^{107}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
25   bromine atom, an iodine atom;  
the C1-C2 alkyl group includes a methyl group, an ethyl group.

          In the representation of  $R^{201}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a

bromine atom, an iodine atom;

the C1-C4 alkyl group includes a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group;

5 the C1-C4 haloalkyl group includes, for example, a fluoromethyl group, a difluoromethyl group, a trifluoromethyl group;

the C1-C4 alkoxy group includes, for example, a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group;

10 the C1-C4 haloalkoxy group includes, for example, a fluoromethoxy group, a difluoromethoxy group, a trifluoromethoxy group, a chloromethyl group, a dichloromethyl group, a trichloromethyl group, a 2,2,2-trifluoroethoxy group, a

15 1,1,2,2-tetrafluoroethoxy group, a 2-fluoroethoxy group;

the di(C1-C4alkyl)amino group includes, for example, a dimethylaminogroup, a diethylaminogroup, a dipropylaminogroup;

In the representation of  $R^{202}$ ,

20 the halogen atom includes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom;

the C1-C4 alkyl group includes, for example, a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group;

25 the C1-C6 haloalkyl group includes, for example, a fluoromethyl group, a difluoromethyl group, a trifluoromethyl group;

the C3-C5 alkylene group represented by  $R^{201}$  and  $R^{202}$  are combined together, for example, a trimethylene group, a tetraethylene group and a pentaethylene group.

In the representation  $R^{203}$  and  $R^{204}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
bromine atom;

the C1-C3 alkyl group includes a methyl group, an ethyl group,  
5 a propyl group and an isopropyl group.

In the representation of  $R^{205}$ ,  
the C1-C4 alkyl group includes a C1-C2 alkyl group such as a  
methyl group, an ethyl group; a propyl group, an isopropyl group,  
a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl  
10 group.

In the representation of  $R^{206}$ ,  $R^{207}$  and  $R^{208}$ ,  
the halogen atom includes a fluorine atom, a chlorine atom, a  
bromine atom, an iodine atom;  
the C1-C2 alkyl group includes a methyl group and an ethyl group.  
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The embodiment of the compound of the present invention  
includes, for example, the following compounds:  
an amide compound represented by formula (1) wherein  $R^{53}$  is a  
hydrogen atom;  
20 an amide compound represented by formula (1) wherein  $R^{62}$ ,  $R^{63}$  and  
 $R^{64}$  are hydrogen atoms;  
an amide compound represented by formula (1) wherein  $R^{58}$  and  $R^{59}$   
are hydrogen atoms;  
an amide compound represented by formula (1) wherein  $R^{56}$  is a  
25 hydrogen atom;  
an amide compound represented by formula (1) wherein  $R^{51}$  is a  
halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a  
C2-C4 alkenyl group, a C2-C4 alkynyl group, a C1-C4 alkoxy group,

a C1-C4 haloalkoxy group, a C1-C4 alkylamino group, a di(C1-C4 alkyl)amino group or a cyano group,  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group or both of  $R^{51}$  and  $R^{52}$  are combined together to be a C3-C5 alkylene group or a group of -CH=CH-CH=CH-;

an amide compound represented by formula (1) wherein  $R^{51}$  is a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group, a C2-C4 alkynyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a C1-C4 alkylamino group, a di(C1-C4 alkyl)amino group or a cyano group;

an amide compound represented by formula (1) wherein  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group;

an amide compound represented by formula (1) wherein  $R^{57}$  is a hydrogen atom or a C1-C3 alkyl group;

an amide compound represented by formula (1) wherein  $R^{60}$  is a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group;

an amide compound represented by formula (1) wherein  $R^{61}$  is a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group;

an amide compound represented by formula (1) wherein  $R^{51}$  is a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a di(C1-C4 alkyl)amino group or a cyano group,  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group or both of  $R^{51}$  and

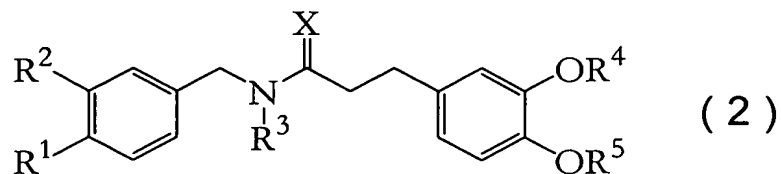


$R^{52}$  are combined together to be a C3-C5 alkylene group or a group of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $R^{53}$  is a hydrogen atom,  $R^{56}$  is a hydrogen atom,  $R^{57}$  is a hydrogen atom, X is an oxygen atom,  $R^{60}$  is a C1-C4 alkyl group,  $R^{61}$  is a C3-C6 alkynyl group;

5 an amide compound represented by formula (1) wherein  $R^{51}$  is a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a di(C1-C4 alkyl)amino group or a cyano group,  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a  
 10 C2-C4 alkenyl group or a C2-C4 alkynyl group or both of  $R^{51}$  and  $R^{52}$  are combined together to be a C3-C5 alkylene group or a group of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $R^{53}$  is a hydrogen atom,  $R^{56}$  is a hydrogen atom,  $R^{57}$  is a hydrogen atom, X is an oxygen atom, each of  $R^{58}$  and  $R^{59}$  is a hydrogen atom, a fluorine atom or a methyl group,  $R^{60}$  is  
 15 a methyl group or an ethyl group,  $R^{61}$  is a C3-C6 alkynyl group,  $R^{62}$ ,  $R^{63}$  and  $R^{64}$  are hydrogen atoms;

an amide compound represented by formula (1) wherein  $R^{51}$  is a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group, a C2-C4 alkynyl group, a C1-C4 alkoxy group,  
 20 a C1-C4 haloalkoxy group, a C1-C4 alkylamino group, a di(C1-C4 alkyl)amino group or a cyano group,  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group or both of  $R^{51}$  and  $R^{52}$  are combined together to be a C3-C6 alkylene group or a group  
 25 of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $R^{53}$  and  $R^{56}$  are hydrogen atoms,  $R^{57}$  is a hydrogen atom or a C1-C3 alkyl group,  $R^{58}$  and  $R^{59}$  are hydrogen atoms,  $R^{60}$  is a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group,  $R^{61}$  is a C1-C4 alkyl group, a

C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group,  $R^{62}$ ,  $R^{63}$  and  $R^{64}$  are hydrogen atoms, namely, the amide compound represented by formula (2):



5 wherein,

$R^1$  represents a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group, a C2-C4 alkynyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a C1-C4 alkylamino group, a di(C1-C4alkyl)amino group or a cyano group;  $R^2$  represents a  
 10 hydrogen atom, a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C2-C4 alkenyl group or a C2-C4 alkynyl group; or both of  $R^1$  and  $R^2$  are combined together to represent a C3-C5 alkylene group or a group of  $-CH=CH-CH=CH-$ ;

$R^3$  represents a hydrogen atom or a C1-C3 alkyl group;

15  $R^4$  represents a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group;

$R^5$  represents a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group;

X represents an oxygen atom or a sulfur atom.

20

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkylamino group;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a halogen atom;

15 an amide compound represented by formula (2) wherein  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom;

20 an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^5$  is a C1-C4 alkyl group;

25 an amide compound represented by formula (2) wherein  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a halogen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^3$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^4$  is a C1-C4 alkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^5$  is a C1-C4 alkyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^5$  is a 2-propynyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a halogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^3$  is a hydrogen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^4$  is a C1-C2 alkyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a halogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^3$  is a hydrogen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^5$  is a C3-C4 alkynyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^5$  is a 2-propynyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a halogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a C1-C4 haloalkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^3$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^4$  is a C1-C4 alkyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C3-C4 alkynyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a halogen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^3$  is a hydrogen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C1-C4 alkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C1-C2 alkyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a halogen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a C1-C4 haloalkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^3$  is a hydrogen atom;

- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^4$  is a C1-C4 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^4$  is a C1-C2 alkyl group;
- 5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C1-C4 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C3-C4 alkynyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C1-C2 alkyl group;
- 10 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a 2-propynyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^2$  is a hydrogen atom;
- 15 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^2$  is a halogen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^2$  is a C1-C4 haloalkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^3$  is a hydrogen atom;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^4$  is a C1-C4 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^4$  is a C1-C2 alkyl group;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^5$  is a C1-C4 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^5$  is a C3-C4 alkynyl group;



an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4alkyl)amino group,  $R^5$  is a 2-propynyl group;

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an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

10

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

15

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

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an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

25

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4

- alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 5 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;  
 10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 15 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl  
 group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 20 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;  
 25 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;  
 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;
- 5 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;
- 10 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;
- 15 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl

group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

- 5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

10

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

15

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

20

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

25

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4

haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$

is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4  
10 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl  
15 group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen  
25 atom,  $R^4$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4



alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,

$R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

15 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

5 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

10 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

20 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group;

25 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a

- trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  
5 atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group;  
an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom;  
an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;  
10 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;  
an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;  
15 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group;  
20 an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group;  
an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group;  
25 an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group;  
an amide compound represented by formula (2) wherein  $R^3$  is a

- hydrogen atom,  $R^5$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^3$  is a  
hydrogen atom,  $R^5$  is a 2-propynyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
5 alkyl group,  $R^5$  is a C1-C4 alkyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a C3-C4 alkynyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a C1-C2 alkyl group;  
10 an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a 2-propynyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a C1-C4 alkyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
15 alkyl group,  $R^5$  is a C3-C4 alkynyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a C1-C2 alkyl group;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a 2-propynyl group;  
20 an amide compound represented by formula (2) wherein  $R^2$  is a  
hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C1-C4 alkyl  
group;  
an amide compound represented by formula (2) wherein  $R^2$  is a  
hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C3-C4 alkynyl  
25 group;  
an amide compound represented by formula (2) wherein  $R^2$  is a  
hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C1-C2 alkyl  
group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C1-C4 alkyl group;  
5 group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C3-C4 alkynyl group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C1-C2 alkyl group;  
10 group;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a 2-propynyl group;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom, X is an oxygen atom;  
15

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group, X is an oxygen atom;  
20

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group, X is an oxygen atom;  
25

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a

- hydrogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^2$  is a halogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;
- 5 an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;
- 10 an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;
- 15 an amide compound represented by formula (2) wherein  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^5$  is a 2-propynyl group, X is an oxygen atom;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a halogen group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a halogen

- atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a halogen  
 atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a halogen  
 5 atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a halogen  
 atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a halogen  
 atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
 10 an amide compound represented by formula (2) wherein  $R^1$  is a halogen  
 atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^2$  is a hydrogen atom, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 15 alkyl group,  $R^2$  is a halogen group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^3$  is a hydrogen atom, X is an oxygen atom;  
 20 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 25 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4



- alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 5 haloalkyl group,  $R^2$  is a hydrogen atom, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a halogen group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen  
 10 atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^3$  is a hydrogen atom, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;  
 15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 20 haloalkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
 haloalkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
 25 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a hydrogen atom, X is an oxygen atom;  
 an amide compound represented by formula (2) wherein  $R^1$  is a  
 chlorine atom,  $R^2$  is a halogen group, X is an oxygen atom;

- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;
- 5 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- 10 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- 15 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a halogen group, X is an oxygen atom;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^3$  is a hydrogen atom, X is an oxygen atom;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a halogen group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^3$  is a hydrogen atom, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen

atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^2$  is a hydrogen atom, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^2$  is a halogen group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^2$  is a C1-C4 haloalkyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^3$  is a hydrogen atom, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a di(C1-C4 alkyl)amino group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

15

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

20

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen

atom,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is  
5 an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
10 alkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group,  
20 X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4  
25 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,

X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl



group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2

alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, 15  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 20 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a

chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$

5 is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4

20 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl

group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

- an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;
- 5 an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a halogen atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;
- 10 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- 15 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 alkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a C1-C4 haloalkyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen

atom;

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

5

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

10

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

15

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

20

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

25

an amide compound represented by formula (2) wherein  $R^1$  is a chlorine atom,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;



- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- 5 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;
- 10 an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a methyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;
- 15 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- 20 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;
- an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;
- 25 an amide compound represented by formula (2) wherein  $R^1$  is a

trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^1$  is a trifluoromethyl group,  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^3$  is a hydrogen atom, X is an oxygen atom;

15 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;

20 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;

25 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^5$  is a 2-propynyl, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^3$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^3$  is a

hydrogen atom,  $R^4$  is a C1-C2 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^3$  is a  
hydrogen atom,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^3$  is a  
5 hydrogen atom,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^3$  is a  
hydrogen atom,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^3$  is a  
hydrogen atom,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
10 an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
15 alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C4  
alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a C1-C4 alkyl group, X is an oxygen atom;  
20 an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a C3-C4 alkynyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
alkyl group,  $R^5$  is a C1-C2 alkyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^4$  is a C1-C2  
25 alkyl group,  $R^5$  is a 2-propynyl group, X is an oxygen atom;  
an amide compound represented by formula (2) wherein  $R^2$  is a  
hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C1-C4 alkyl  
group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C3-C4 alkynyl group, X is an oxygen atom;

5 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C2 alkyl group,  $R^4$  is a 2-propynyl group, X is an oxygen atom;

10 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C3-C4 alkynyl group, X is an oxygen atom;

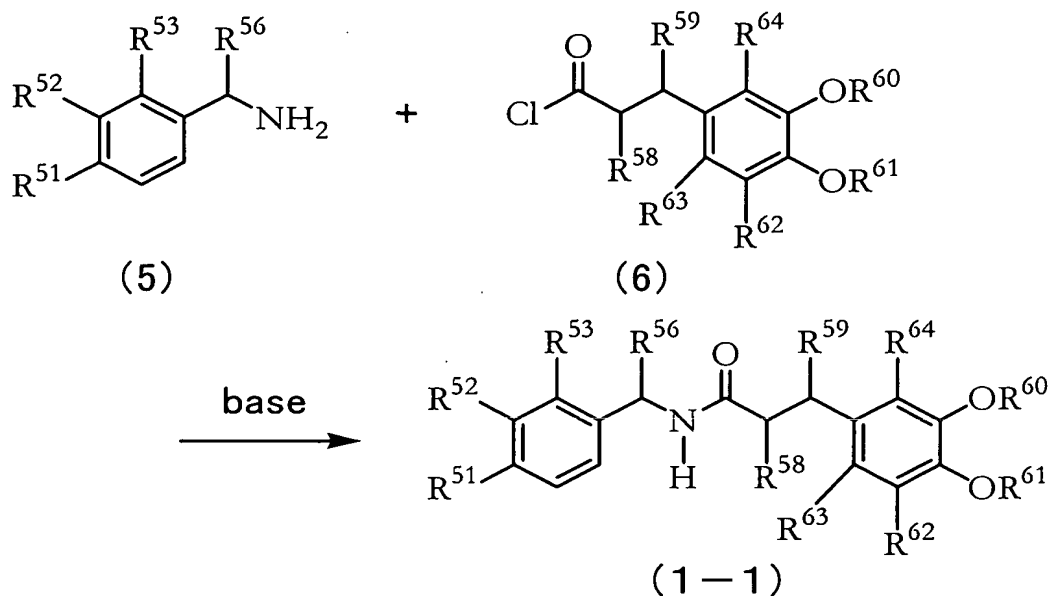
15 an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a C1-C4 alkyl group, X is an oxygen atom;

an amide compound represented by formula (2) wherein  $R^2$  is a hydrogen atom,  $R^4$  is a C1-C4 alkyl group,  $R^4$  is a 2-propynyl group, X is an oxygen atom.

Next, production methods for the compounds of the present invention are described. The compounds of the present invention can be produced, for example, according to the following (Production Method A), (Production Method B), (Production Method C) or (Production Method D).

(Production Method A)

The compound (1-1) among the compound of the present invention wherein  $R^{57}$  is a hydrogen atom and X is an oxygen atom can be produced by making the compound (5) react with the compound (6).



5

wherein, in the formula,

$R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{56}$ ,  $R^{58}$ ,  $R^{59}$ ,  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$  and  $R^{64}$  represent same meaning as described above.

The reaction is carried out usually in the presence of a solvent and usually in the presence of a base.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide

15

and the mixture thereof.

The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, tertiary amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like, nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

The molar ratio applied to the base is usually from 1 to 10 moles per 1 mole of the compound (6) and that to the compound (5) is usually from 1 to 5 moles.

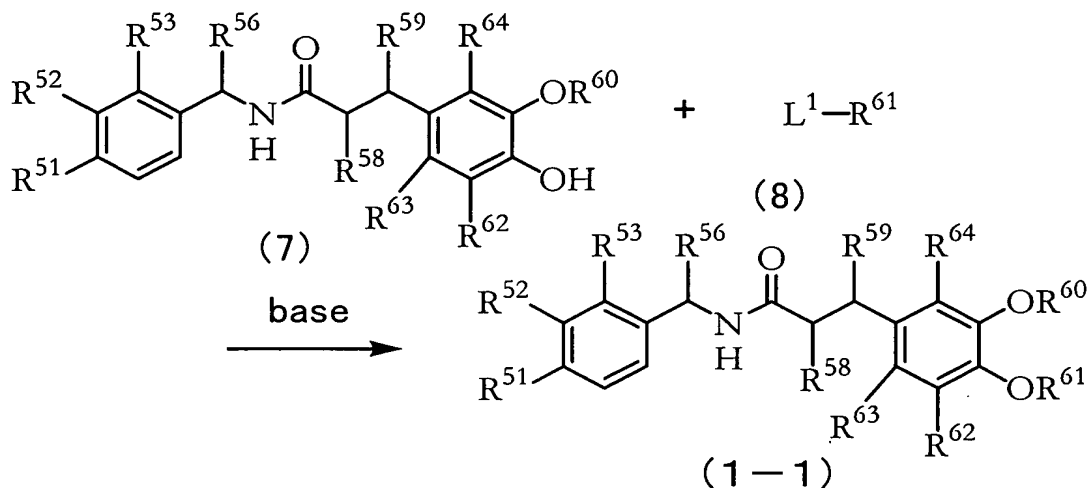
The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (1-1) can be isolated by subjecting to post-treatment such as (i) the reaction mixture is poured into water, extracted with organic solvent; the organic layer is washed with acidic water (diluted hydrochloric acid and the like), basic water (aqueous solution of sodium bicarbonate and the like), if necessary; then the organic layer is dried and concentrated, or (ii) to the reaction mixture small amount of water is added, and concentrated under reduced pressure, then the obtained solid is collected by filtration. The isolated compound (1-1) can be purified by a technique such as chromatography, recrystallization and the like.

(Production Method B)

The compound (1-1) among the compound of the present invention wherein  $R^{57}$  is a hydrogen atom and X is an oxygen atom

can be also produced by making the compound (7) react with the compound (8).



wherein, in the formula,

- 5  $L^1$  represents a halogen atom, a methansulfonyloxy group, a trifluoromethanesulfonyloxy group or a p-toluenesulfonyloxy group,  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{56}$ ,  $R^{58}$ ,  $R^{59}$ ,  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$  and  $R^{64}$  represent same meaning as described above.

10 The reaction is carried out usually in the presence of a solvent and usually in the presence of a base.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like,  
 15 aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide  
 20 and the mixture thereof.

The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, alkali metal hydrides such as sodium hydride, potassium hydride and the like, tertiary amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like, nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

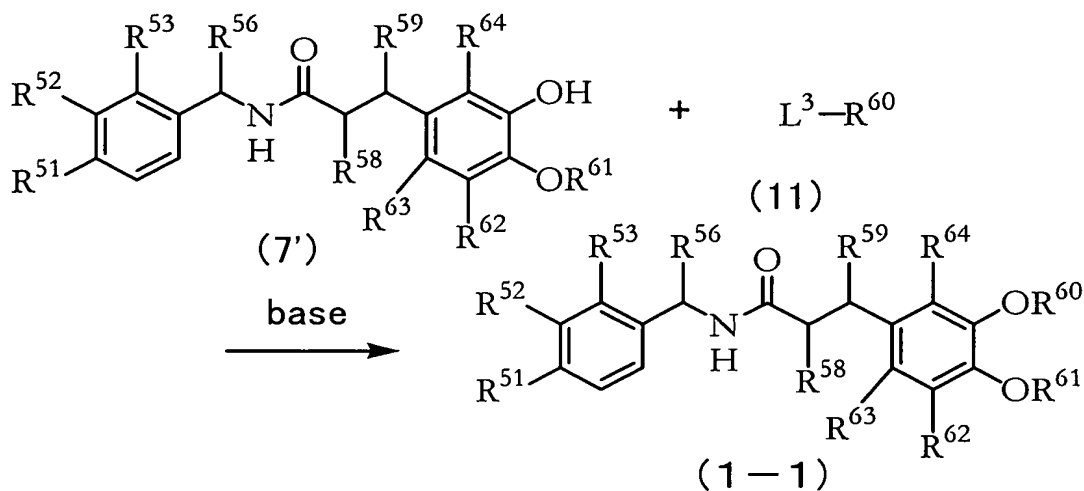
The molar ratio applied to the base is usually from 1 to 10 moles per 1 mole of the compound (7) and that to the compound (8) is usually from 1 to 5 moles.

The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (1-1) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, extracted with organic solvent; the organic layer is washed with acidic water (diluted hydrochloric acid and the like), basic water (aqueous solution of sodium bicarbonate and the like), if necessary; then the organic layer is dried and concentrated. The isolated compound (1-1) can be purified by a technique such as chromatography, recrystallization and the like.

Further, the compound (1-1) can be also produced by making the compound (7') react with the compound (11).





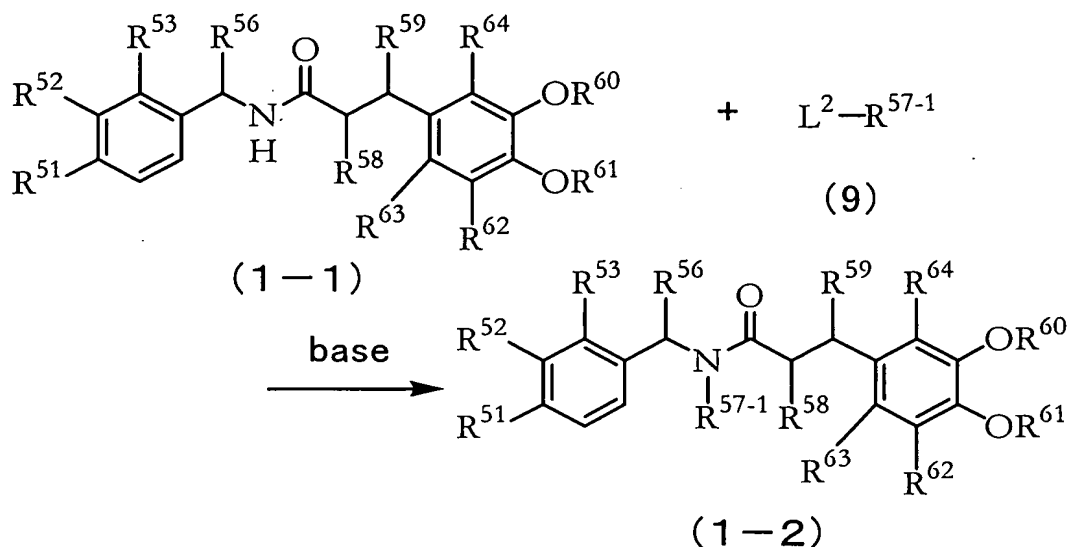
wherein, in the formula,

L<sup>3</sup> represents a halogen atom, a methanesulfonyloxy group, a trifluoromethanesulfonyloxy group or a p-toluenesulfonyloxy group, R<sup>51</sup>, R<sup>52</sup>, R<sup>53</sup>, R<sup>56</sup>, R<sup>58</sup>, R<sup>59</sup>, R<sup>60</sup>, R<sup>61</sup>, R<sup>62</sup>, R<sup>63</sup> and R<sup>64</sup> represent same meaning as described above.

The reaction is carried out in a similar condition as the above mentioned reaction.

(Production Method C)

10 The compound (1-2) among the compound of the present invention wherein R<sup>57</sup> is a C1-C4 alkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group and X is an oxygen atom can be produced by making the compound (1-1) react with the compound (9).



wherein, in the formula,

L<sup>2</sup> represents a halogen atom, a methanesulfonyloxy group, a trifluoromethanesulfonyloxy group or a p-toluenesulfonyloxy group, R<sup>57-1</sup> represents a C1-C4 alkyl group, a C3-C4 alkenyl group or a C3-C4 alkynyl group, R<sup>51</sup>, R<sup>52</sup>, R<sup>53</sup>, R<sup>56</sup>, R<sup>58</sup>, R<sup>59</sup>, R<sup>60</sup>, R<sup>61</sup>, R<sup>62</sup>, R<sup>63</sup> and R<sup>64</sup> represent same meaning as described above.

The reaction is carried out usually in the presence of a solvent and usually in the presence of a base.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide and the mixture thereof.

The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, alkali metal hydrides such as sodium hydride potassium hydride and the like, tertiary amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like, nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

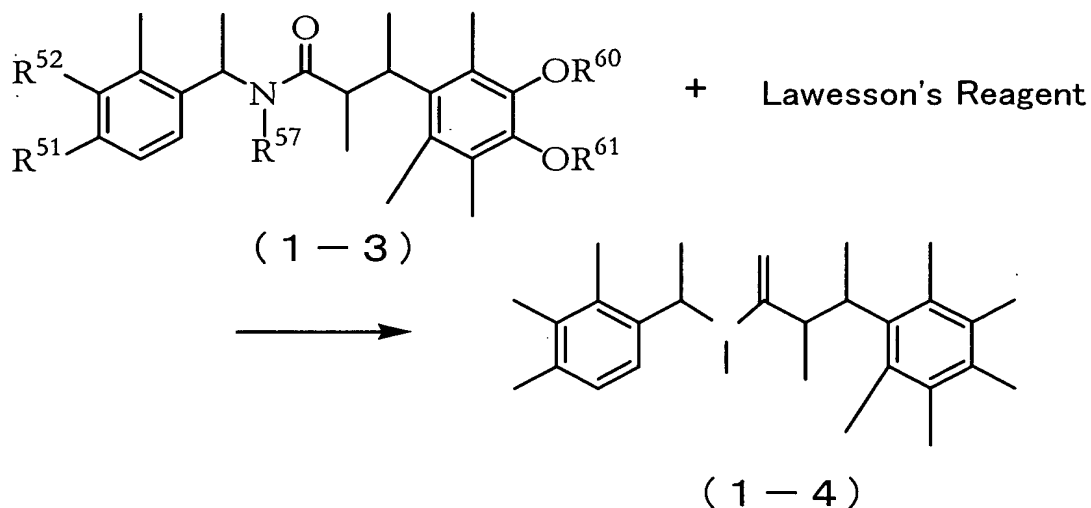
The molar ratio applied to the base is usually from 1 to 10 moles per 1 mole of the compound (1-1) and that to the compound (9) is usually from 1 to 5 moles.

The reaction temperature is usually in the range of from 0 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (1-2) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (1-2) can be purified by a technique such as chromatography, recrystallization and the like.

(Production Method D)

The compound (1-4) among the compound of the present invention wherein X is a sulfur atom can be produced by making the compound (1-3), which X is an oxygen atom among the compound of the present invention, react with 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-diisulfide (which is generally known as "Lawesson's Reagent").



ran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, nitriles such as acetonitrile, butyronitrile and the like, sulfoxides such as dimethyl sulfoxide and the mixture thereof.

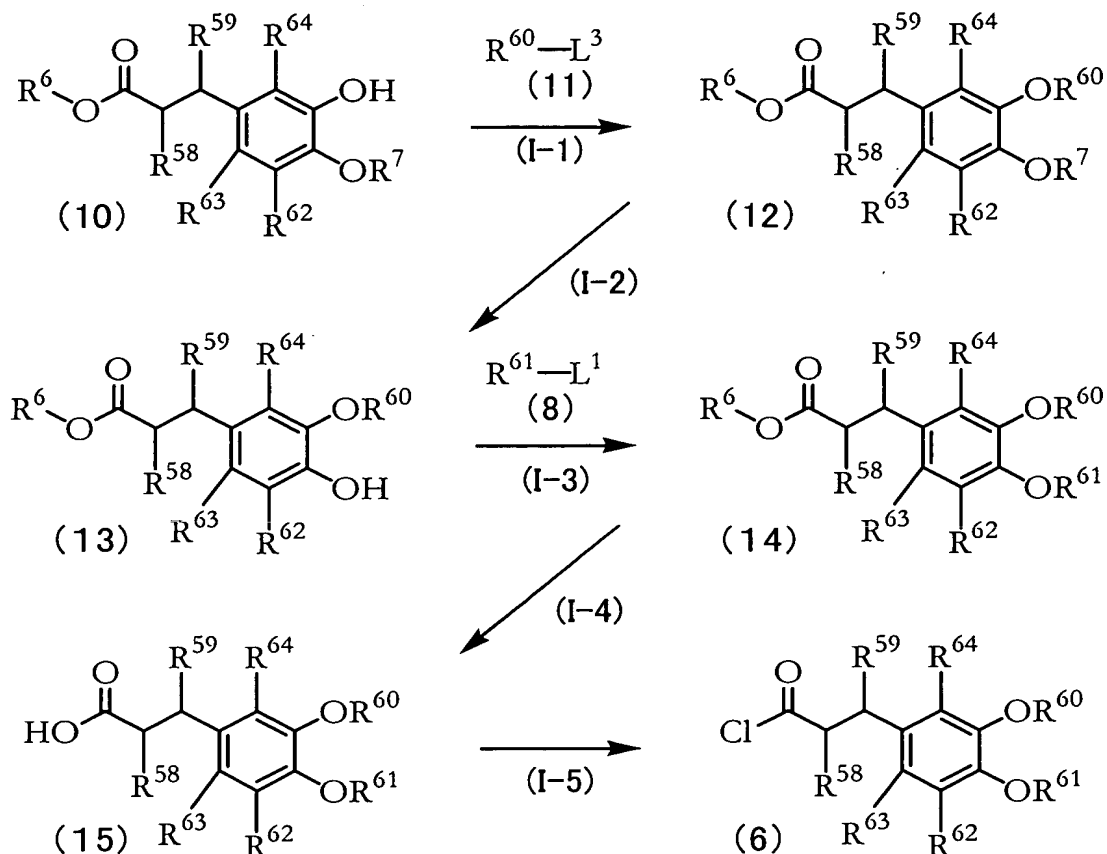
The molar ratio applied to the Lawesson's Reagent is usually from 1 to 10 moles per 1 mole of the compound (1-3).

The reaction temperature is usually in the range of from 50 to 150 °C, and the reaction time is usually in the range of from 0.5 to 24 hours.

After completion of the reaction, the compound (1-4) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (1-4) can be purified by a technique such as chromatography, recrystallization and the like.

Next, production methods for the intermediate compounds for the present invention are described.

The compound (6) can be produced, for example, according to following scheme.



wherein, in the formula,

- 5  $R^6$  represents a C1-C6 alkyl group,  $R^7$  represents a benzyl group or a methoxymethyl group,  $R^{58}, R^{59}, R^{60}, R^{61}, R^{62}, R^{63}, R^{64}, L^1$  and  $L^3$  represent same meaning as described above.

Step(I-1)

- 10 The compound (12) can be produced by making the compound (10) react with the compound (11).

The reaction is carried out in the presence of a solvent or absence of a solvent, and usually in the presence of a base.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol

dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide and the mixture thereof.

The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, alkali metal hydrides such as sodium hydride potassium hydride and the like, tertiary amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like, nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

The molar ratio applied to the base is usually from 1 to 50 moles per 1 mole of the compound (10) and that to the compound (11) is usually from 1 to 5 moles.

The reaction temperature is usually in the range of from 0 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (12) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (12) can be purified by a technique such as chromatography, recrystallization and the like.

The compound (10) is, for example, the compound described in Tetrahedron Letters, vol.36, No.51, pp.9369-9372, 1995 or can be produced according to similar methods described in that literature.

5 Step(I-2)

(A) In case of  $R^7$  is a benzyl group

The compound (13) can be produced by making the compound (12) react with hydrogen in the presence of a hydrogenation catalyst and an acid.

10 The reaction is carried out usually under hydrogen atmosphere and usually in the presence of a solvent.

The solvent used for the reaction includes, for example, alcohols such as methanol, ethanol, propanol and the like, esters such as ethyl acetate, butyl acetate and the like, ethers such  
15 as tetrahydrofuran, 1,4-dioxane and the like and the mixture thereof.

The hydrogenation catalyst used for the reaction includes, for example, transition metal compounds such as palladium charcoal, palladium hydroxide, Raney nickel, platinum oxide and  
20 the like. The acid used for the reaction includes, for example, hydrochloric acid.

The molar ratio applied to hydrogen is 1 mole per 1 mole of the compound (13) and that to the hydrogenation catalyst is usually from 0.001 to 0.5 moles.

25 The reaction is usually carried out under hydrogen atmosphere of from 1 to 100 atoms.

The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of

from 0.1 to 24 hours.

After completion of the reaction, the compound (13) can be isolated by subjecting to post-treatment such as the reaction mixture is filtered, and the filtrate is extracted with organic solvent, then the obtained organic layer is dried and concentrated. The isolated compound (13) can be purified by a technique such as chromatography, recrystallization and the like.

(B) In case of  $R^7$  is a methoxymethyl group

The compound (11) can be produced by subjecting the compound (12) to hydrolysis reaction in the presence of an acid.

The reaction is usually carried out in the presence of water and an organic solvent.

The organic solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide, alcohols such as methanol, ethanol, propanol and the like and the mixture thereof.

The acid used for the reaction includes, for example, inorganic acids such as hydrochloric acid, sulfuric acid and the like, organic acids such as p-toluenesulfonic acid, methansulfonic acid and the like.

The molar ratio applied to the acid is usually from 1 to



10 moles per 1 mole of the compound (12).

The reaction temperature is usually in the range of from 0 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

5        After completion of the reaction, the compound (13) can be isolated by subjecting to post-treatment such as the reaction mixture is extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (13) can be purified by a technique such as chromatography, recrystallization  
10       and the like.

#### Step(I-3)

The compound (14) can be produced by making the compound (13) react with the compound (8).

15       The reaction is carried out in the presence of a solvent or absence of a solvent, and usually in the presence of a base.

20       The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide  
25       and the mixture thereof.

The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, tertiary amines such as triethylamine,

diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like, nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

5           The molar ratio applied to the base is usually from 1 to 50 moles per 1 mole of the compound (13) and that to the compound (8) is usually from 1 to 5 moles.

          The reaction temperature is usually in the range of from 0 to 100 °C, and the reaction time is usually in the range of  
10       from 0.1 to 24 hours.

          After completion of the reaction, the compound (14) can be isolated by subjecting to post-treatment such as following: after adding an organic solvent to the reaction mixture if necessary, the reaction mixture is filtered and the filtrate is  
15       concentrated. The isolated compound (14) can be purified by a technique such as distillation, chromatography, recrystallization and the like.

#### Step(I-4)

          The compound (15) can be produced by subjecting the  
20       compound (14) to hydrolysis reaction in the presence of a base.

          The reaction is usually carried out in the presence of water and an organic solvent.

          The organic solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like,  
25       aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, nitriles such as acetonitrile, butyronitrile and the like, alcohols such as

methanol, ethanol, propanol and the like and the mixture thereof.

The base used for the reaction includes, for example, alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide and the like.

5           The molar ratio applied to the base is usually from 1 to 10 moles per 1 mole of the compound (14).

The reaction temperature is usually in the range of from 0 to 150 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

10           After completion of the reaction, the compound (15) can be isolated by subjecting to post-treatment such as acidic water (hydrochloric acid and the like) is added to the reaction mixture, and the mixture is extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (15) can  
15 be purified by a technique such as distillation, chromatography, recrystallization and the like.

Step(I-5)

The compound (6) can be produced by making the compound (15) react with a chlorinating agent.

20           The reaction is carried out in the presence of a solvent or absence of a solvent.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic  
25 hydrocarbons such as hexane, heptane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene and the mixture thereof.

The chlorinating agent used for the reaction includes,

for example, thionyl chloride, oxalyl chloride, phosphorus oxychloride.

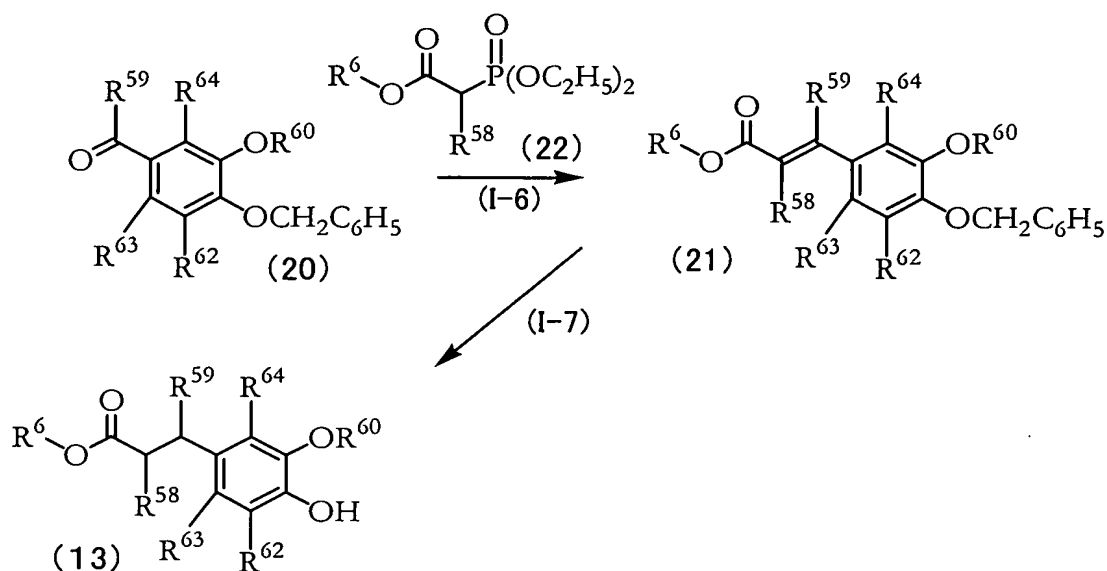
The molar ratio applied to the chlorinating agent is usually from 1 to 100 moles per 1 mole of the compound (15).

5        The reaction temperature is usually in the range of from 30 to 150 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (6) can be isolated by subjecting to post-treatment such as the reaction  
10        mixture is concentrated. The isolated compound (6) usually can be used to the reaction of next step without further purification.

The compound in the compound (14) wherein  $R^{60}$  is a C1-C4 alkyl group,  $R^{61}$  is a C3-C6 alkynyl group,  $R^6$  is a methyl group, an ethyl group, a propyl group, an isopropyl group, an isobutyl  
15        group, a tert-butyl group; the compound in the compound (15) wherein  $R^{60}$  is a methyl group or an ethyl group,  $R^{61}$  is a C3-C6 alkynyl group; and the compound which is described the formula (6) wherein  $R^{60}$  is a methyl group or an ethyl group,  $R^{61}$  is a C3-C6 alkynyl group,  $R^{58}$ ,  $R^{59}$ ,  $R^{62}$ ,  $R^{63}$  and  $R^{64}$  are hydrogen atoms, are  
20        the intermediate 1 of the present invention.

The compound (13) can also be produced by according to following scheme.



wherein, in the formula,

$\text{R}^6$  represents a C1-C6 alkyl group,  $\text{R}^7$  represents a benzyl group or a methoxymethyl group,  $\text{R}^{58}$ ,  $\text{R}^{59}$ ,  $\text{R}^{60}$ ,  $\text{R}^{62}$ ,  $\text{R}^{63}$ ,  $\text{R}^{64}$ ,  $\text{L}^1$  and  $\text{L}^3$  represent same meaning as described above.

#### Step(I-6)

The compound (21) can be produced by making the compound (20) react with the compound (22) described below and a base.

The reaction is carried out in the presence of a solvent.

The solvent used for the reaction includes, for example, tetrahydrofuran. The base used to the reaction includes carbonates such as potassium carbonate and the like, alkali metal hydrides such as sodium hydride and the like.

The molar ratio applied to the compound (22) is usually from 1 to 2 moles per 1 mole of the compound (20) and that to the base is usually from 1 to 2 moles. The reaction temperature is usually in the range of from 0 to 80 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (20) can

be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, and extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (20) can be purified by a technique such as chromatography, recrystallization and the like.

The compound (20) is commercially available or can be produced in the similar manner as well known methods.

#### Step(I-7)

The compound (13) can be produced by making the compound (20) react with hydrogen in the presence of a hydrogenation catalyst and an acid.

The solvent used for the reaction includes, for example, alcohols such as methanol, ethanol, propanol and the like, esters such as ethyl acetate, butyl acetate and the like, ethers such as tetrahydrofuran, 1,4-dioxane and the like and the mixture thereof.

The hydrogenation catalyst used for the reaction includes, for example, transition metal compounds such as palladium charcoal, palladium hydroxide, Raney nickel, platinum oxide and the like. The acid used for the reaction includes, for example, hydrochloric acid.

The molar ratio applied to hydrogen is usually 2 moles per 1 mole of the compound (13) and that to the hydrogenation catalyst is usually from 0.01 to 0.5 moles.

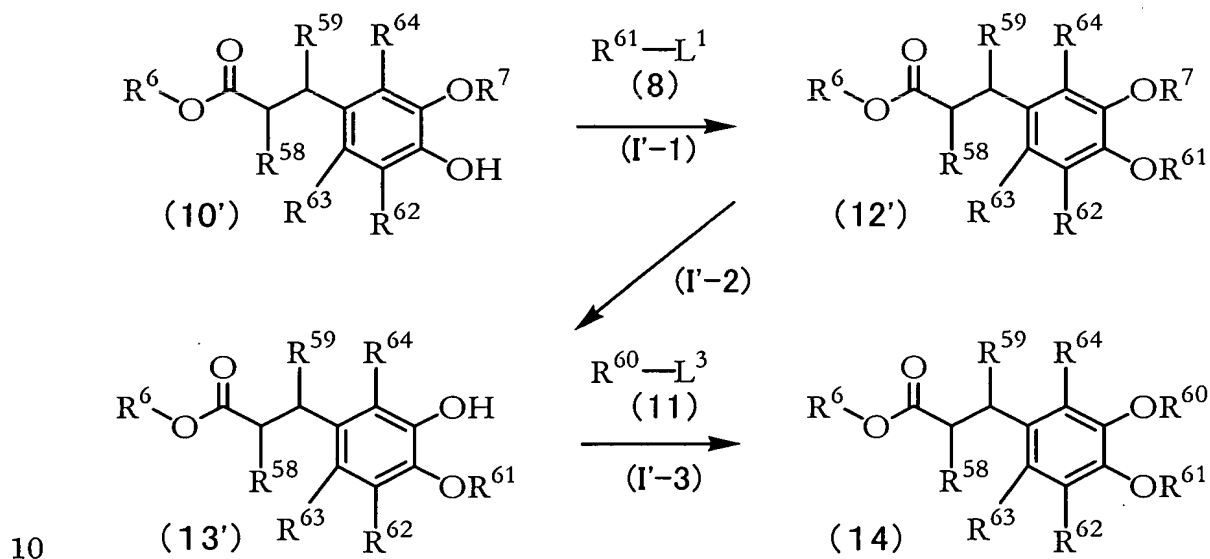
The reaction is usually carried out under hydrogen atmosphere of from 1 to 100 atmos.

The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of

from 0.1 to 24 hours.

After completion of the reaction, the compound (13) can be isolated by subjecting to post-treatment such as the reaction mixture is filtered, and the filtrate is extracted with organic solvent, then the obtained organic layer is dried and concentrated. The isolated compound (13) can be purified by a technique such as chromatography, recrystallization and the like.

The compound (14) can also be produced by according to following scheme.



wherein, in the formula,

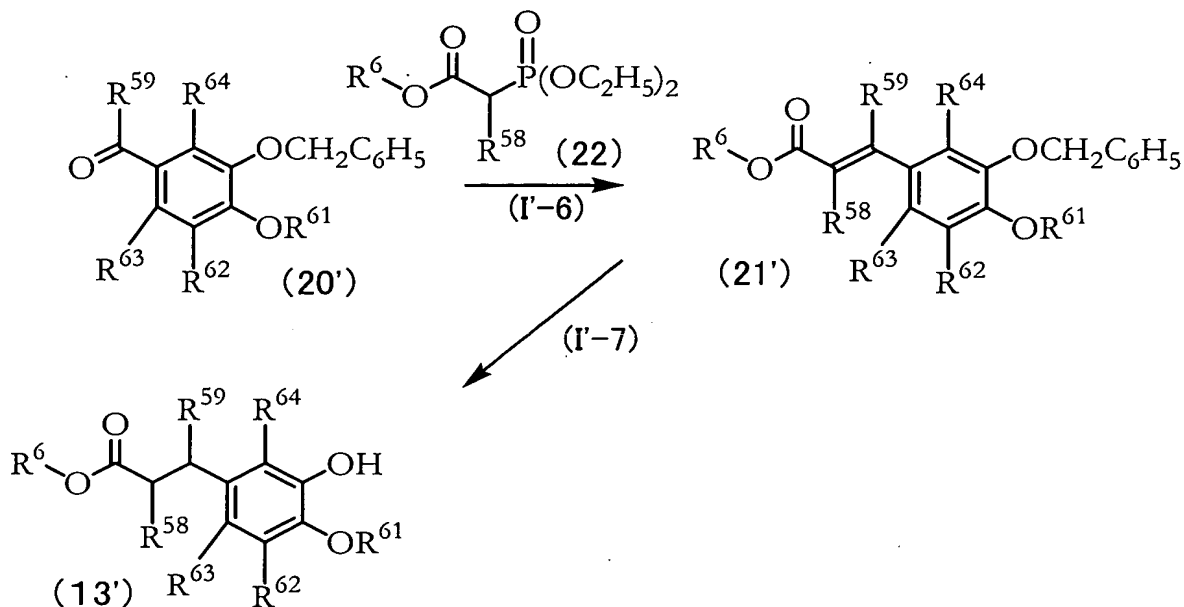
$R^6$  represents a C1-C6 alkyl group,  $R^7$  represents a benzyl group or a methoxymethyl group,  $R^{58}$ ,  $R^{59}$ ,  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$ ,  $L^1$  and  $L^3$  represent same meaning as described above.

15 Step(I'-1) can be carried out in a similar manner as Step(I-3) described above. Step(I'-2) can be carried out in a similar manner as Step(I-2) described above. Step(I'-3) is similar condition as Step(I-1).

The compound (10') is, for example, the compound described

in Tetrahedron Letters, vol.36, No.51, pp.9369-9372, 1995 or can be produced according to similar methods described in that literature.

The compound (13') can also be produced by according to following scheme.



wherein, in the formula,

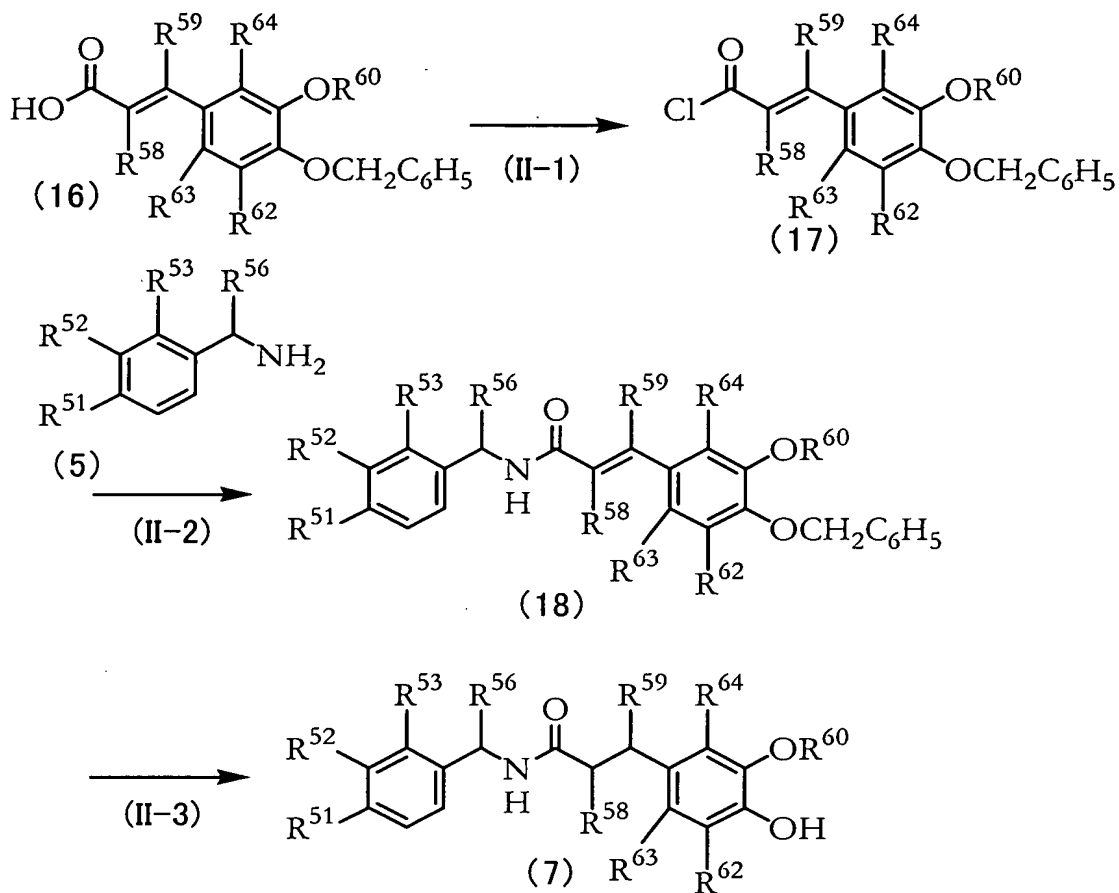
R<sup>6</sup> represents a C1-C6 alkyl group, R<sup>7</sup> represents a benzyl group or a methoxymethyl group, R<sup>58</sup>, R<sup>59</sup>, R<sup>61</sup>, R<sup>62</sup>, R<sup>63</sup>, R<sup>64</sup>, L<sup>1</sup> and L<sup>3</sup> represent same meaning as described above.

Step(I'-6) can be carried out in a similar manner as Step(I-6) described above. Step(I'-7) can be carried out in a similar manner as Step(I-7) described above.

The compound (20') is commercially available or can be produced by in a similar manner as well known methods.

The compound (7) can be produced, for example, by according to following scheme.





wherein, in the formula,

$R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{56}$ ,  $R^{58}$ ,  $R^{59}$ ,  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$  represent same meaning as described above.

#### 5 Step(II-1)

The compound (17) can be produced by making the compound (16) react with a chlorinating agent.

The reaction is carried out in the presence of a solvent or absence of a solvent.

10

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated

hydrocarbons such as chlorobenzene and the mixture thereof.

The chlorinating agent used for the reaction includes, for example, thionyl chloride, oxalyl chloride and phosphorus oxychloride.

5           The molar ratio applied to the chlorinating agent is usually from 1 to 100 moles per 1 mole of the compound (16).

The reaction temperature is usually in the range of from 30 to 150 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

10           After completion of the reaction, the compound (17) can be isolated by subjecting to post-treatment such as the reaction mixture is concentrated. The isolated compound (17) usually can be used to the reaction of next step without further purification.

15           The compound (16) is, for example, the compound described in Synthetic Communications, 29(4), pp.573-581(1999) or can be produced according to similar methods described in that literature.

Step(II-2)

20           The compound (18) can be produced by making the compound (17) react with the compound (5).

The reaction is carried out usually in the presence of a solvent and usually in the presence of a base.

25           The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as

ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide and the mixture thereof.

5           The base used for the reaction includes, for example, carbonates such as sodium carbonate, potassium carbonate and the like, tertiary amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene and the like,  
10       nitrogen-contained aromatic compounds such as pyridine, 4-dimethylaminopyridine.

          The molar ratio applied to the base is usually from 1 to 10 moles per 1 mole of the compound (17) and that to the compound (5) is usually from 1 to 5 moles.

15           The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

          After completion of the reaction, the compound (18) can be isolated by subjecting to post-treatment such as (i) the  
20       reaction mixture is poured into water, extracted with organic solvent; the organic layer is washed with acidic water (diluted hydrochloric acid and the like), basic water (aqueous solution of sodium bicarbonate and the like), if necessary; then the organic layer is dried and concentrated, or (ii) to the reaction mixture  
25       small amount of water is added, and concentrated under reduced pressure, then the obtained solid is collected by filtration. The isolated compound (18) can be purified by a technique such as chromatography, recrystallization and the like.

## Step(II-3)

The compound (7) can be produced by making the compound (18) react with hydrogen in the presence of a hydrogenation catalyst and an acid.

5        The reaction is carried out usually under hydrogen atmosphere and usually in the presence of a solvent.

      The solvent used for the reaction includes, for example, alcohols such as methanol, ethanol, propanol and the like, esters such as ethyl acetate, butyl acetate and the like, ethers such as tetrahydrofuran, 1,4-dioxane and the like and the mixture thereof.

10       The hydrogenation catalyst used for the reaction includes, for example, transition metal compounds such as palladium charcoal, palladium hydroxide, Raney nickel, platinum oxide and the like.

15       The acid used for the reaction includes, for example, such as hydrochloric acid.

      The molar ratio applied to hydrogen is usually 2 moles per 1 mole of the compound (18) and that to the hydrogenation catalyst is usually from 0.001 to 0.5 moles.

20       The reaction is usually carried out under hydrogen atmosphere of from 1 to 100 atoms.

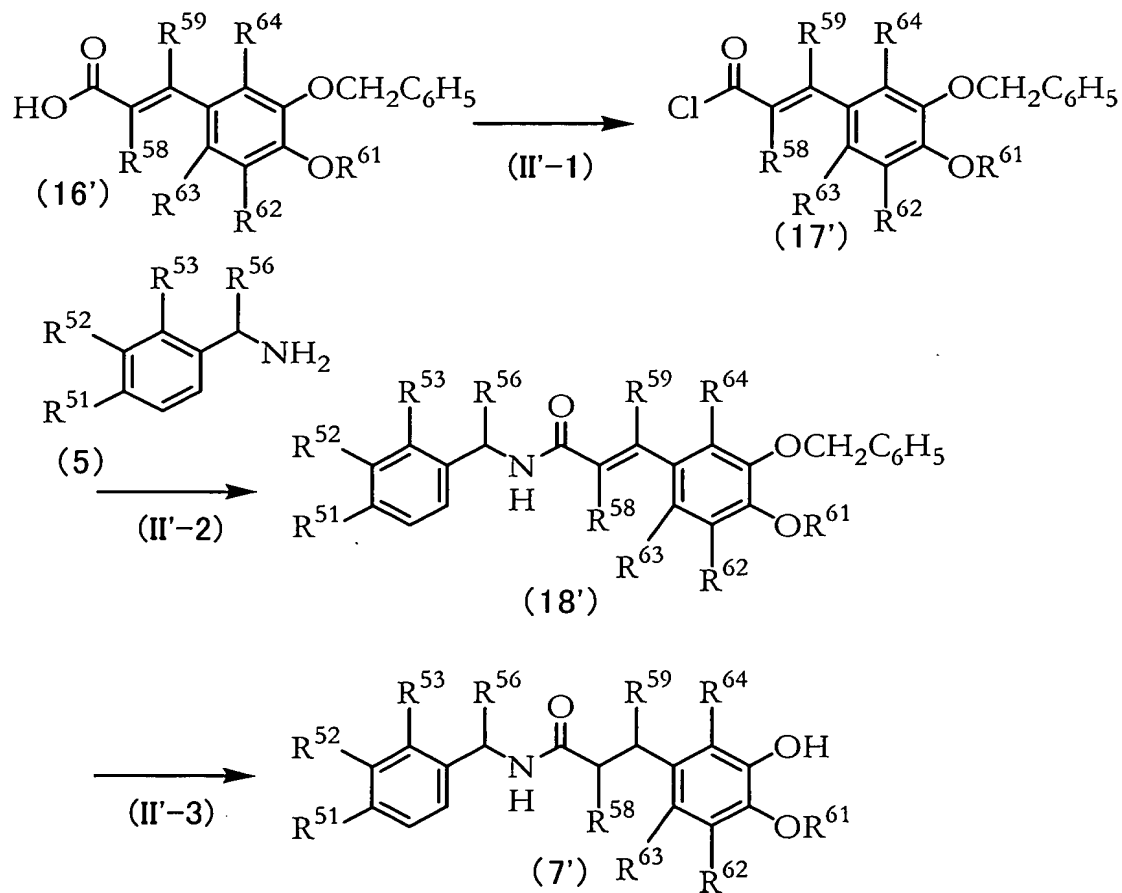
      The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

25       After completion of the reaction, the compound (7) can be isolated by subjecting to post-treatment such as the reaction mixture is filtered, and the filtrate is extracted with organic solvent, then the obtained organic layer is dried and concentrated.

The isolated compound (7) can be purified by a technique such as chromatography, recrystallization and the like.

The compound in the compound (7) wherein  $R^{51}$  is a halogen atom, a C1-C4 alkyl group, a C1-C4 haloalkyl group, a C1-C4 alkoxy group, a C1-C4 haloalkoxy group, a di(C1-C4 alkyl)amino group or a cyano group,  $R^{52}$  is a hydrogen atom, a halogen atom, a C1-C4 alkyl group or a C1-C4 haloalkyl group; or both of  $R^{51}$  and  $R^{52}$  are combined together to be a C3-C5 alkylene group or a group of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $R^{53}$  is a hydrogen atom,  $R^{56}$  is a hydrogen atom,  $R^{60}$  is a C1-C4 alkyl group, is the intermediate 2 of the present invention.

The compound (7') can be produced, for example, by according to following scheme.

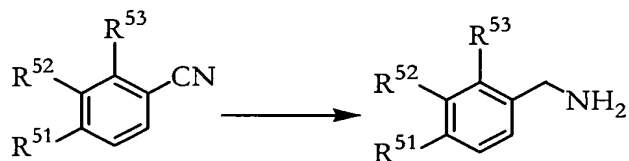


$R^{51}, R^{52}, R^{53}, R^{56}, R^{58}, R^{59}, R^{60}, R^{61}, R^{62}, R^{63}, R^{64}$  represent same meaning as described above.

5

10

The compound (5-1) among the compound (5) wherein R<sup>56</sup> is a hydrogen atom can be produced, for example, by subjecting the compound (19) to reduction reaction.



15

wherein, in the formula,

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> represent same meaning as described above.

The reaction is usually carried out in the presence of a solvent.

20

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like and

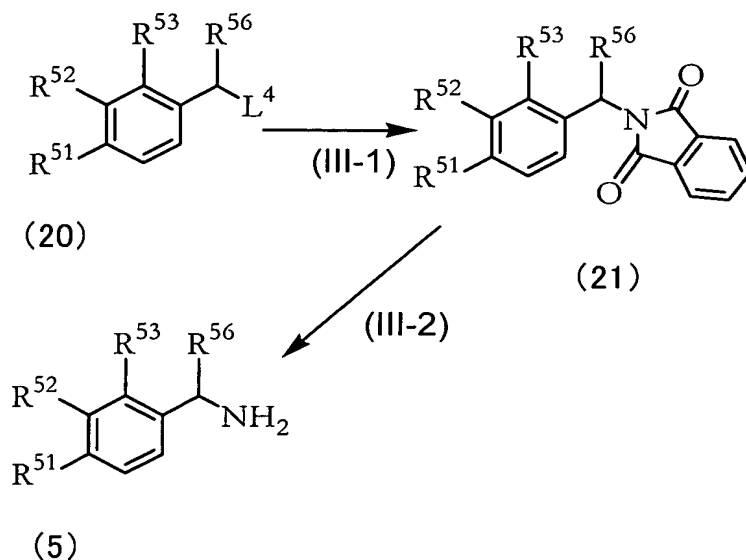
the mixture thereof.

The reducing agent used for the reaction includes, for example, metal hydrides such as lithium aluminium hydride, diisobutyl aluminium hydride.

5        The molar ratio applied to the reducing agent is usually from 0.5 to 5 moles per 1 mole of the compound (19), but it is changeable depend on the kind of reducing agent .

After completion of the reaction, the compound (5) can be isolated by subjecting to post-treatment such as the reaction  
 10 mixture is poured into water, extracted with organic solvent; the organic layer washed with basic water (aqueous solution of sodium hydroxide and the like) if necessary, then dried and concentrated. The isolated compound (5) can be purified by a technique such as distillation, chromatography and the like.

15        The compound (5) can be produced by according to following scheme.



wherein, in the formula,

$R^{51}$ ,  $R^{52}$ ,  $R^{53}$  and  $R^{56}$  represent same meaning as described above,

L<sup>4</sup> represents a chlorine atom or a bromine atom.

Step(III-1)

The compound (21) can be produced by making the compound (20) react with potassium phthalimide.

5 The reaction is usually carried out in the presence of a solvent.

The solvent used for the reaction includes ethers such as 1,4-dioxane, tetrahydrofuran, ethyleneglycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide, 10 water and the mixture thereof.

The molar ratio applied to potassium phthalimide is usually from 1 to 3 moles per 1 mole of the compound (20).

The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of 20 from 0.1 to 24 hours.

After completion of the reaction, the compound (21) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water and extracted with organic solvent; the organic layer is dried and concentrated. The isolated 25 compound (21) can be purified by a technique such as chromatography, recrystallization and the like.

Step(III-2)

The compound (5) can be produced by making the compound



(21) react with hydrazine.

The reaction is usually carried out in the presence of a solvent.

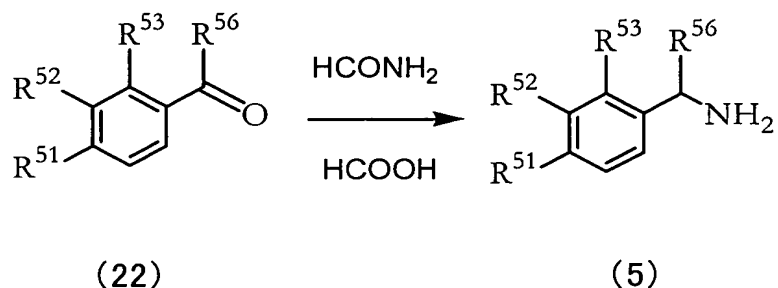
The solvent used for the reaction includes alcohols such as methanol, ethanol, propanol and the like, water and the mixture thereof.

Hydrazine used for the reaction may be its hydrate. The molar ratio applied to hydrazine is usually from 1 to 10 moles per 1 mole of the compound (21).

The reaction temperature is usually in the range of from 0 to 150 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (5) can be isolated by subjecting to post-treatment such as the reaction mixture is filtered, water is added to the filtrate, and extracted with organic solvent; then the organic layer is dried and concentrated. The isolated compound (5) can be purified by a technique such as distillation, chromatography and the like.

The compound (5) can be produced, for example, by subjecting the compound (22) to Leuckart Reaction.



wherein, in the formula,

R<sup>51</sup>, R<sup>52</sup>, R<sup>53</sup>, and R<sup>56</sup> represent same meaning as described above.

The reaction is carried out in the presence of a solvent

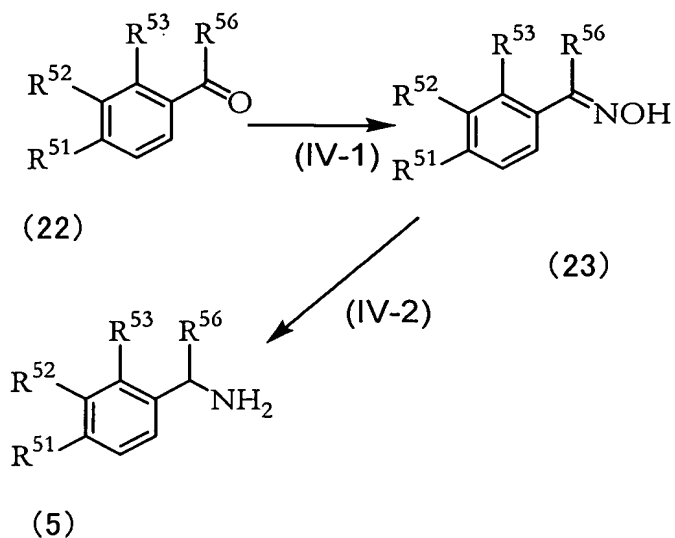
or absence of solvent, in the presence of formamide and formic acid.

The solvent used for the reaction includes, for example, ethers such as 1,4-dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like and the mixture thereof.

The molar ratio applied to formamide is usually from 1 to 15 moles per 1 mole of the compound (22), and that to formic acid is usually from 0.1 to 2 moles.

After completion of the reaction, the compound (5) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, extracted with organic solvent; if necessary, the organic layer washed with basic water (aqueous solution of sodium hydroxide and the like); then dried and concentrated. The isolated compound (5) can be purified by a technique such as distillation, chromatography and the like.

The compound (5) can be produced by according to following scheme.



wherein, in the formula,

$R^{51}$ ,  $R^{52}$ ,  $R^{53}$ , and  $R^{56}$  represent same meaning as described above.

Step(VI-1)

5           The compound (23) can be produced by making the compound (22) react with hydroxyl amine.

The reaction is usually carried out in the presence of a solvent.

10           The solvent used for the reaction includes ethers such as 1,4-dioxane, tetrahydrofuran, ethyleneglycol dimethylether, tert-butyl methyl ether and the like, aliphatic hydrocarbons such as hexane, heptane, octane and the like, aromatic hydrocarbons such as toluene, xylene and the like, halogenated hydrocarbons such as chlorobenzene, esters such as ethyl acetate, butyl acetate and the like, nitriles such as acetonitrile, butyronitrile and the like, acid amides such as N,N-dimethylformamide, sulfoxides such as dimethyl sulfoxide, alcohols such as methanol, ethanol, propanol, isopropanol and the like, water and the mixture thereof.

20           The molar ratio applied to hydroxyl amine is usually from

1 to 5 moles per 1 mole of the compound (22).

The reaction temperature is usually in the range of from 0 to 150 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

5           After completion of the reaction, the compound (23) can be isolated by subjecting to post-treatment such as the reaction mixture is poured into water, and extracted with organic solvent, then the organic layer is dried and concentrated. The isolated compound (23) can be purified by a technique such as chromatography,  
10           recrystallization and the like.

#### Step(VI-2)

The compound (5) can be produced by making the compound (23) react with hydrogen in the presence of a hydrogenation catalyst.

15           The reaction is usually carried out under hydrogen atmosphere, and usually in the presence of a solvent.

The solvent used for the reaction includes, for example, alcohols such as methanol, ethanol, propanol and the like, esters such as ethyl acetate, butyl acetate and the like, ethers such  
20           as tetrahydrofuran, 1,4-dioxane and the like and the mixture thereof.

The hydrogenation catalyst used for the reaction includes, for example, transition metal compounds such as palladium charcoal, palladium hydroxide, Raney nickel, platinum oxide and  
25           the like.

The molar ratio applied to hydrogen is usually 2 moles per 1 mole of the compound (23) and that to the hydrogenation catalyst is usually from 0.001 to 0.5 moles.

The reaction is usually carried out under hydrogen atmosphere of from 1 to 100 atoms. The reaction can be carried out by added an acid (hydrochloric acid and the like), if necessary.

5 The reaction temperature is usually in the range of from -20 to 100 °C, and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, the compound (5) can be isolated by subjecting to post-treatment such as the reaction mixture is filtered, and the filtrate is extracted with organic solvent, then the obtained organic layer is dried and concentrated.  
10 The isolated compound (5) can be purified by a technique such as chromatography, recrystallization and the like.

Plant diseases against which the compound of the present invention has controlling activity include, for example, a  
15 disease due to Phycomycetes, specifically following diseases are illustrated:

*Peronospora brassicae* of vegetables and radishes; *Peronospora spinaciae* of spinach; *Peronospora tabacina* of tobacco;  
*Pseudoperonospora cubensis* of gourds; *Plasmopara viticola* of  
20 grapes; *Phytophthora cactorum* of apple, strawberry and ginseng;  
*Phytophthora capsici* of tomato and cucumber; *Phytophthora cinnamomi* of pineapple; *Phytophthora infestans* of potato and tomato;  
*Phytophthora nicotianae* var. *nicotianae* of tobacco, broad bean and leek; *Pythium* sp. of spinach; *Pythium aphanidermatum* of  
25 cucumber; *Pythium* sp. of wheat; *Pythium debaryanum* of tobacco; and *Pythium* rot of soybean (*Pythium aphanidermatum*, *P. debaryanum*, *P. irregulare*, *P. myriotylum*, *P. ultimum*).

The compound of the present invention can control plant

diseases by applying for plants or soils growing the plant as it is. But usually it is used a composition which contains the compound of the present invention and a carrier, namely it is a form of plant diseases controlling composition which the compound of the present invention is held by proper carrier. The plant diseases controlling composition of the present invention is a formulation such as emulsifiable concentrate, wettable powder, dry flowable, flowable, dust, granule and the like; obtained by mixing the compound of the present invention, and solid carrier, a liquid carrier, surfactant and other adjuvant for formulation. These formulations usually contain 0.1 to 90 % by weight of the compound of the present invention.

Solid carriers used for formulation include, for example, fine powders or granules of minerals such as kaolin clay, attapulgite clay, bentonite, montmorillonite, terra alba, pyrophyllite, talc, diatomaceous earth, calcite and the like; natural organic substances such as corncob powder, walnut shell powder and the like; synthetic organic substances such as urea and the like; salts such as calcium carbonate, ammonium sulfate and the like; synthetic inorganic substances such as synthetic hydrous silicon oxide and the like. Liquid carriers include, for example, aromatic hydrocarbons such as xylene, alkylbenzene, methylnaphthalene and the like; alcohols such as 2-propanol, ethylene glycol, propylene glycol, cellosolve and the like; ketones such as acetone, cyclohexanone, isophorone and the like; vegetable oils such as soybean oil, cottonseed oil and the like; aliphatic hydrocarbons, esters, dimethylsulfoxide, acetonitrile and water.

Surfactants include, for example, anionic surfactants such as alkylsulfuric acid ester salt, alkylarylsulfonic acid salt, dialkylsulfosuccinic acid salt, polyoxyethylenealkylaryletherphosphoric acid ester salt, lignin sulfonic acid salt, polycondensed naphthalenesulfonateformaldehyde and the like; and nonionic surfactants such as polyoxyethylenealkylarylether, polyoxyethylenealkylpolyoxypropyleneblockcopolymer, sorbitan fatty acid ester and the like.

Another adjuvant for formulation includes, for example, water-soluble polymers such as polyvinylalcohol, polyvinylpyrrolidone and the like; Arabian gum; alginic acid and its salt thereof; polysaccharides such as CMC(carboxymethylcellulose), xanthangum and the like; inorganic substances such as alminum magnesium silicate, alumina sol and the like; and preservatives, colorants, PAP(isopropyl acidic phosphate), stabilizing agents such as BHT and the like.

By applying the plant diseases controlling composition of the present invention to treatment for foliage of plants, said plants can be protected from plant diseases; and by applying the plant diseases controlling composition of the present invention to treatment for soils, the plants grown on said soils can be protected from plant diseases.

When the plant diseases controlling composition of the present invention is applied to foliage treatment for plants or soil treatment, the application amount thereof, which may be varied with a kind of control-object plants, a kind of control-object disases, an infestation level of control-object

diseases, formulation types, application timings, weather conditions and the like, is usually 1 to 5000 g, preferably 5 to 1000 g, of the compound of the present invention per 10,000 m<sup>2</sup>.

5           Emulsifiable concentrate, wettable powder, flowable and the like are usually sprayed after diluted with water. In this case, the concentration of the compound of the present invention is usually in the range of from 0.0001 to 3 % by weight, preferably from 0.0005 to 1 % by weight. Dust, granule and the like are  
10 usually directly applied without dilution.

          The plant diseases controlling composition of the present invention can be also applied in treatment methods such as seed disinfection and the like. The methods include, for example, a method to soak seeds of a plant in the plant diseases controlling  
15 composition of the present invention which prepared in 1 to 1,000 ppm in terms of concentration of the compound of the present invention, a method to spray or coat seeds of a plant with the liquid plant diseases controlling composition of the present  
invention which prepared in 1 to 1,000 ppm in terms of concentration  
20 of the compound of the present invention, and a method to coat seeds of a plant with the plant diseases controlling composition of the present invention which is formulated to dust.

          The method for controlling plant diseases of the present invention is usually performed by applying effective amount of  
25 the composition of the present invention to a plant or a soil growing the plant in which infection is predictable and/or to a plant or a soil growing the plant in which infection is confirmed.

          The plant diseases controlling composition of the present



invention is usually used as an agent controlling plant diseases for agriculture or gardening, that is, as an agent controlling plant diseases to control plant diseases on plowed fields, paddy fields, orchards, tea fields, pastures, lawn and the like.

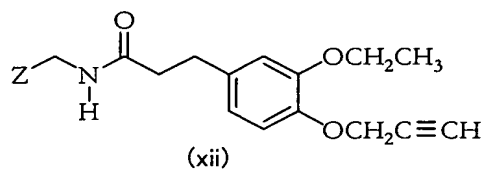
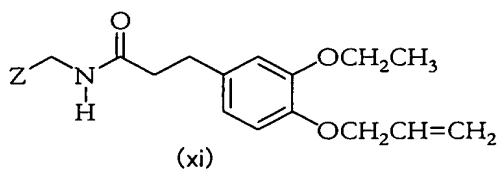
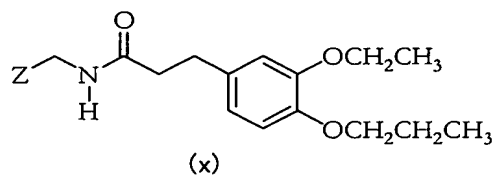
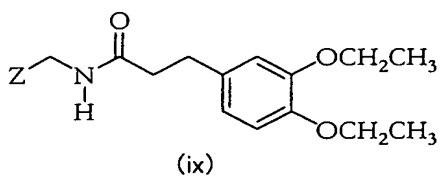
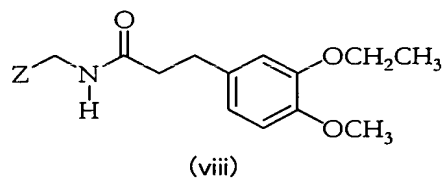
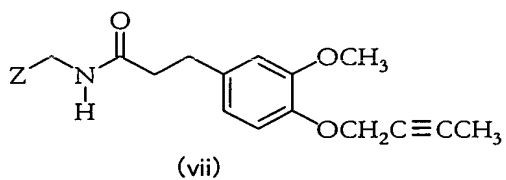
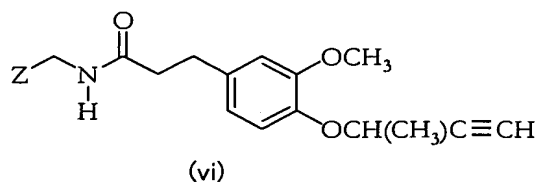
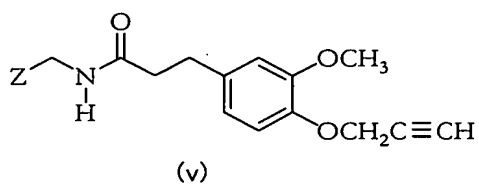
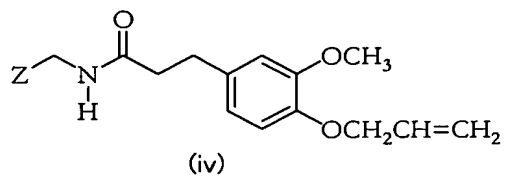
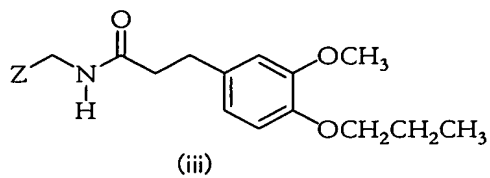
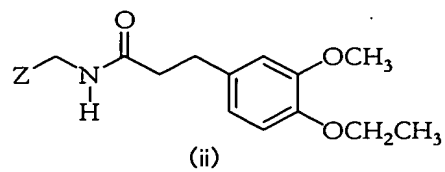
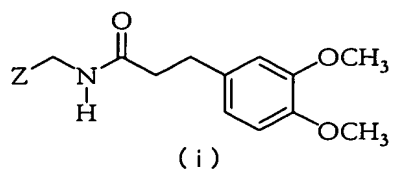
5           The plant diseases controlling composition of the present invention may be used together with other plant disease controlling compositions, pesticides, acaricides, nematocides, herbicides, plant growth regulators and/or fertilizers.

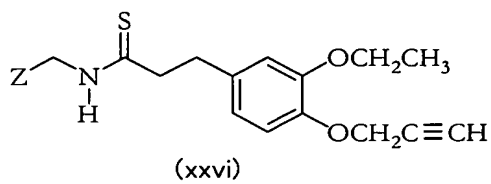
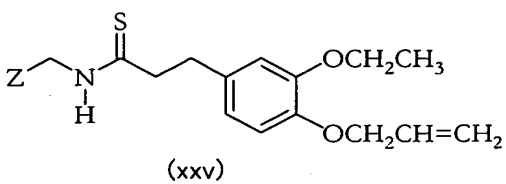
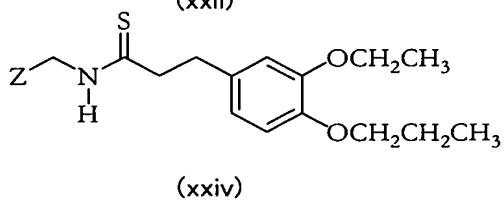
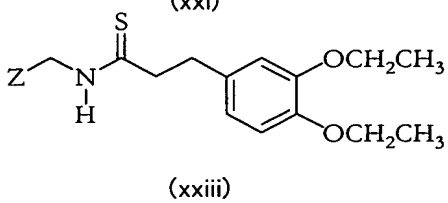
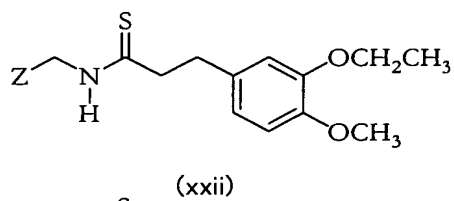
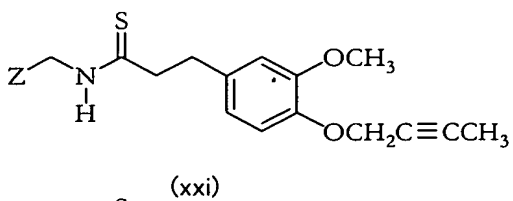
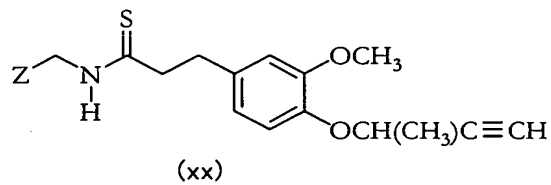
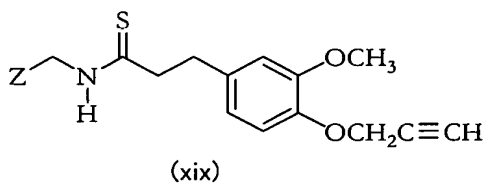
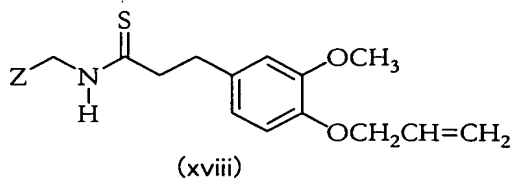
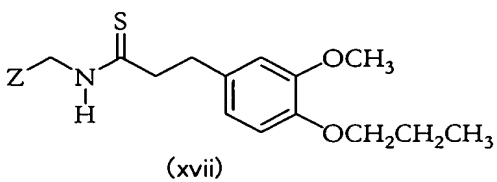
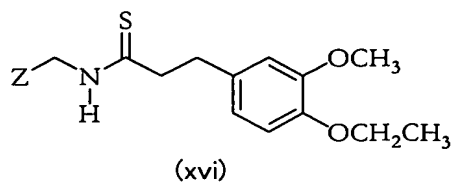
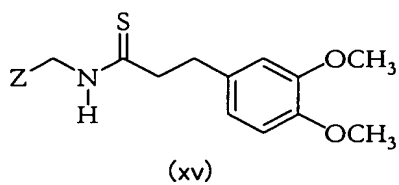
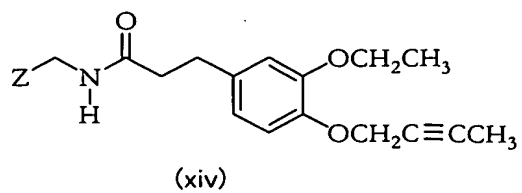
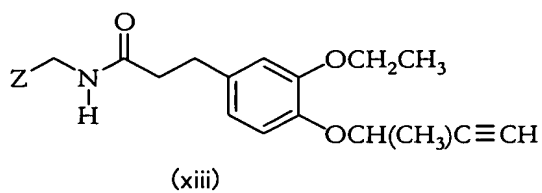
10           Examples of the active ingredient of such other plant diseases controlling composition include:

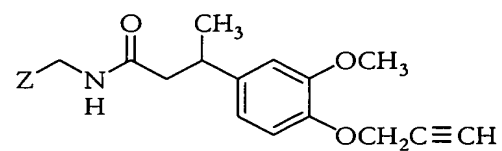
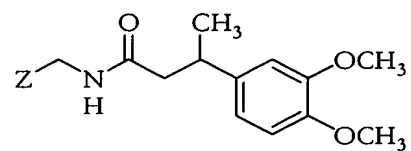
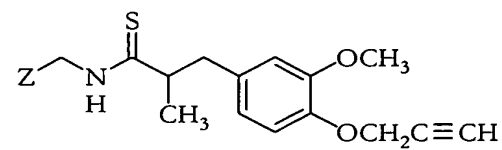
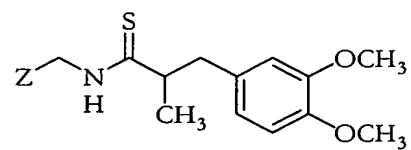
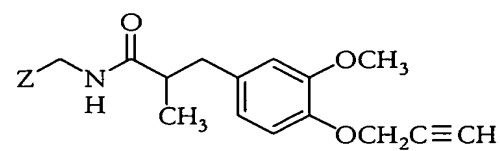
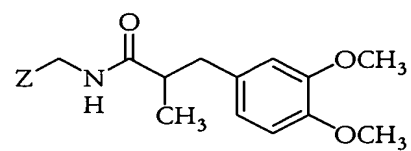
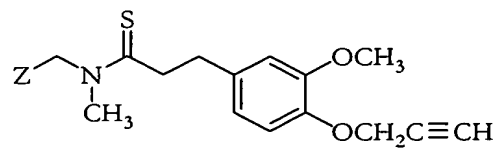
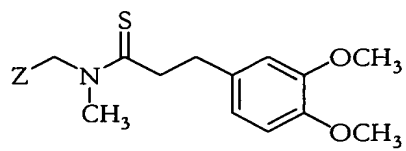
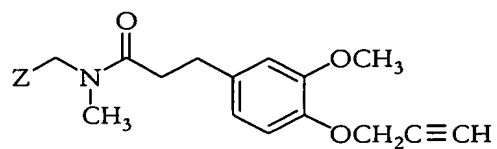
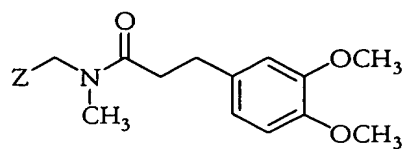
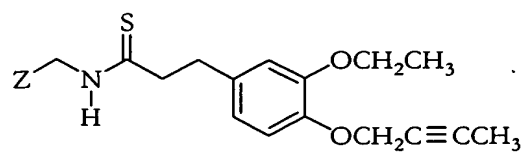
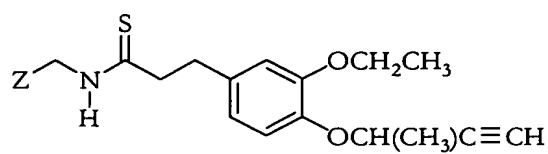
chlorothalonil; fluazinam; dichlofluanid; fosetyl-Al; cyclic imide derivatives such as captan, captafol, folpet and the like; dithiocarbamate derivatives such as maneb, mancozeb, thiuram, ziram, zineb, propineb and the like; inorganic or organic copper derivatives such as basic copper sulfate, basic copper chloride, copper hydroxide, copper-oxinate and the like; acylalanine derivatives such as metalaxyl, furalaxyl, ofurace, cyprofuram, benalaxyl, oxadixyl and the like; strobilurine like compound such as kresoxim-methyl, azoxystrobin, trifloxystrobin, 15 picoxystrobin, pyraclostrobin, dimoxystrobin and the like; anilinopyrimidine derivatives such as cyprodinil, pyrimethanil, mepanipyrim and the like; phenyl pyrrole derivatives such as fenpiclonil, fludioxonil and the like; imide derivatives such as procymidone, iprodione, vinclozolin and the like; 20 benzimidazole derivatives such as carbendazim, benomyl, thiabendazole, thiophanatemethyl and the like; amine derivatives such as fenpropimorph, tridemorph, fenpropidin, spiroxamine and the like; azole derivatives such as propiconazole, triadimenol,

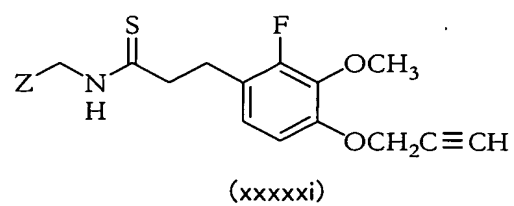
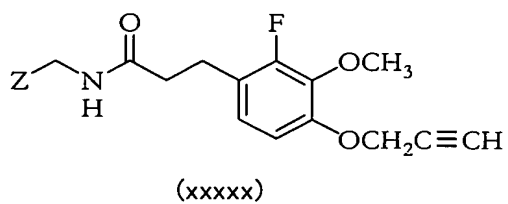
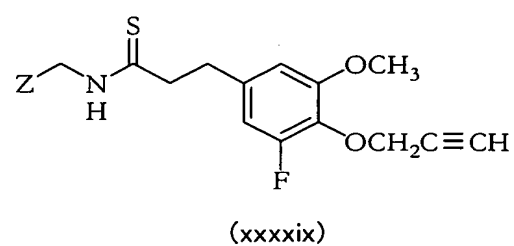
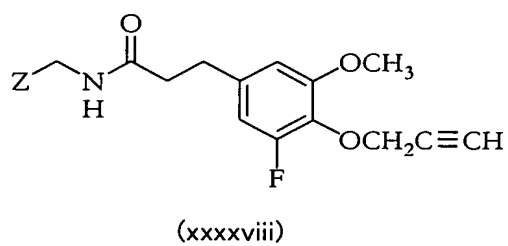
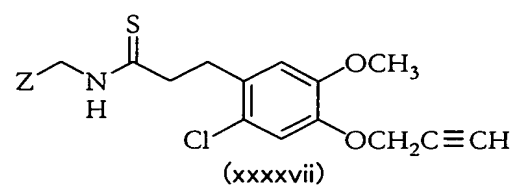
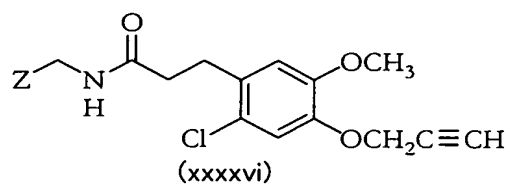
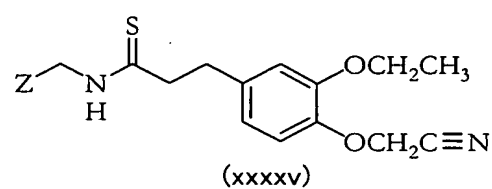
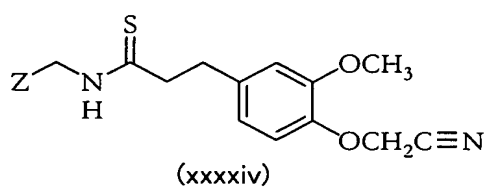
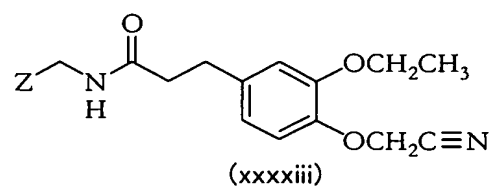
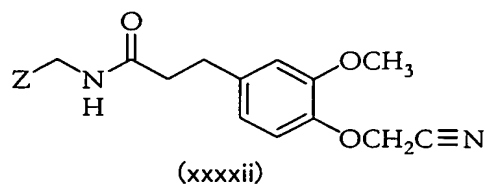
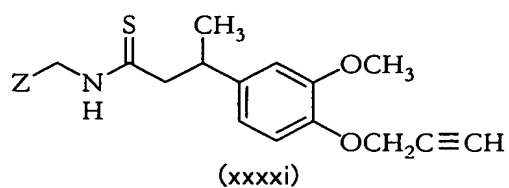
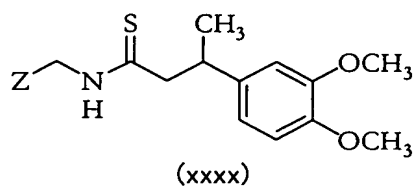
prochloraz, penconazole, tebuconazole, flusilazole,  
diniconazole, bromuconazole, epoxiconazole, difenoconazole,  
cyproconazole, metconazole, triflumizole, tetraconazole,  
myclobutanil, fenbuconazole, hexaconazole, fluquinconazole,  
5 triticonazole, bitertanol, imazalil, flutriafol and the like;  
cymoxanil; dimethomorph; famoxyadone, fenamidone;  
iprovalicarb; benthiavalicarb; cyazofamid, zoxamide,  
ethaboxam; nicobifen; fenhexamid; quinoxifen; diethofencarb and  
acibenzolar S-methyl.

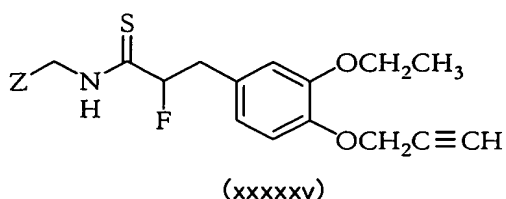
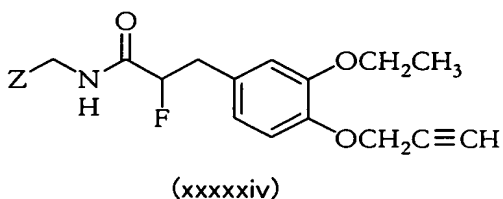
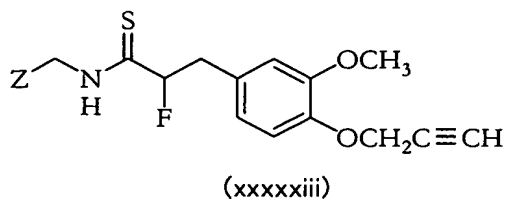
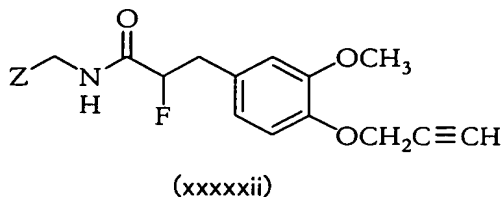
10           Specific examples of the compound of the present invention  
are described below:  
amide compounds shown by formula(i) to (xxxxxv)











In formula (i) to (xxxxxv), Z represents any one of group below:

- 4-fluorophenyl group, 4-chlorophenyl group, 4-bromophenyl group,
- 5 4-iodophenyl group, 4-methylphenyl group, 4-ethylphenyl group,
- 4-propylphenyl group, 4-isopropylphenyl group, 4-butylphenyl group,
- 4-(sec-butyl)phenyl group, 4-isobutylphenyl group,
- 4-(tert-butyl)phenyl group, 4-vinylphenyl group,
- 4-(1-methylvinyl)phenyl group, 4-(1-propenyl)phenyl group,
- 10 4-(2-methyl-1-propenyl)phenyl group, 4-(1-butenyl)phenyl group,
- 4-ethynylphenyl group, 4-(1-propynyl)phenyl group,
- 4-(1-butyryl)phenyl group, 4-(1-pentanylyl)phenyl group,
- 4-(3-methyl-1-butyryl)phenyl group,
- 4-(3,3-dimethyl-1-butyryl)phenyl group,
- 15 4-(fluoromethyl)phenyl group, 4-(difluoromethyl)phenyl group,
- 4-(trifluoromethyl)phenyl group, 4-methoxyphenyl group,
- 4-ethoxyphenyl group, 4-(fluoromethoxy)phenyl group,
- 4-(difluoromethoxy)phenyl group, 4-(trifluoromethoxy)phenyl group,
- 4-cyanophenyl group, 4-(N,N-dimethylamino)phenyl group,
- 20 4-(N,N-diethylamino)phenyl group, 4-(N,N-dipropylamino)phenyl group,
- group, 3,4-difluorophenyl group, 4-chloro-3-fluorophenyl group,
- 4-bromo-3-fluorophenyl group, 3-fluoro-4-methylphenyl group,

	4-ethyl-3-fluorophenyl	group,
	3-fluoro-4-(trifluoromethyl)phenyl	group,
	3-fluoro-4-methoxyphenyl group, 4-cyano-3-fluorophenyl group,	
	4-fluoro-3-chlorophenyl group, 3,4-dichlorophenyl group,	
5	4-bromo-3-chlorophenyl group, 3-chloro-4-methylphenyl group,	
	3-chloro-4-ethylphenyl	group,
	3-chloro-4-(trifluoromethyl)phenyl	group,
	3-chloro-4-methoxyphenyl group, 4-cyano-3-chlorophenyl group,	
	3-bromo-4-fluorophenyl group, 3-bromo-4-chlorophenyl group,	
10	3,4-dibromophenyl group, 3-bromo-4-methylphenyl group,	
	3-bromo-4-ethylphenyl	group,
	3-bromo-4-(trifluoromethyl)phenyl	group,
	3-bromo-4-methoxyphenyl group, 3-bromo-4-cyanophenyl group,	
	4-fluoro-3-methylphenyl group, 4-chloro-3-methylphenyl group,	
15	4-chloro-3-methylphenyl group, 3,4-dimethylphenyl group,	
	4-ethyl-3-methylphenyl	group,
	3-methyl-4-(trifluoromethyl)phenyl	group,
	4-methoxy-3-methylphenyl group, 4-cyano-3-methylphenyl group,	
	3-ethyl-4-fluoromethyl group, 4-chloro-3-ethylphenyl group,	
20	4-bromo-3-ethylphenyl group, 3-ethyl-4-methylphenyl group,	
	3,4-diethylphenyl group, 3-ethyl-4-(trifluoromethyl)phenyl	
	group, 3-ethyl-4-methoxyphenyl group, 4-cyano-3-ethylphenyl	
	group, 4-fluoro-3-(trifluoromethyl)phenyl	group,
	4-chloro-3-(trifluoromethyl)phenyl	group,
25	4-bromo-3-(trifluoromethyl)phenyl	group,
	4-methyl-3-(trifluoromethyl)phenyl	group,
	4-ethyl-3-(trifluoromethyl)phenyl	group,
	3,4-di-(trifluoromethyl)phenyl	group,



- 4-methoxy-3-(trifluoromethyl)phenyl group,  
 4-cyano-3-(trifluoromethyl)phenyl group,  
 4-methoxycarbonylphenyl group, 4-ethoxycarbonylphenyl group,  
 4-phenylphenyl group, 3-fluoro-4-phenylphenyl group,  
 5 3-chloro-4-phenylphenyl group, 3-bromo-4-phenylphenyl group,  
 3-methyl-4-phenylphenyl group, 3-ethyl-4-phenylphenyl group,  
 4-phenoxyphenyl group, 3-fluoro-4-phenoxyphenyl group,  
 3-chloro-4-phenoxyphenyl group, 3-bromo-4-phenoxyphenyl group,  
 3-methyl-4-phenoxyphenyl group, 3-ethyl-4-phenoxyphenyl group,  
 10 4-nitrophenyl group, 3-fluoro-4-nitrophenyl group,  
 3-chloro-4-nitrophenyl group, 3-bromo-4-nitrophenyl group,  
 3-methyl-4-nitrophenyl group, 3-ethyl-4-nitrophenyl group,  
 4-methylthiophenyl group, 3-fluoro-4-methylthiophenyl group,  
 3-chloro-4-methylthiophenyl group, 3-bromo-4-methylthiophenyl  
 15 group, 3-methyl-4-methylthiophenyl group,  
 3-ethyl-4-methylthiophenyl group,  
 Indan-5-yl group, 5,6,7,8-tetrahydronaphthalene-2-yl group,  
 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl group,  
 5,6,7,8,9,10-hexahydro-benzocyclooctene-2-yl group,  
 20 2-naphthyl group, 4-fluoronaphthalene-2-yl group,  
 5-fluoronaphthalene-2-yl group, 6-fluoronaphthalene-2-yl group,  
 7-fluoronaphthalene-2-yl group, 4-chloronaphthalene-2-yl group,  
 5-chloronaphthalene-2-yl group, 6-chloronaphthalene-2-yl group,  
 7-chloronaphthalene-2-yl group, 4-bromonaphthalene-2-yl group,  
 25 5-bromonaphthalene-2-yl group, 6-bromonaphthalene-2-yl group,  
 7-bromonaphthalene-2-yl group, 4-methylnaphthalene-2-yl group,  
 5-methylnaphthalene-2-yl group, 6-methylnaphthalene-2-yl group,  
 7-methylnaphthalene-2-yl group, 4-methoxynaphthalene-2-yl

	group,	5-methoxynaphthalene-2-yl	group,
	6-methoxynaphthalene-2-yl	group,	7-methoxynaphthalene-2-yl
	group,	4-trifluoromethylnaphthalene-2-yl	group,
	5-trifluoromethylnaphthalene-2-yl		group,
5	6-trifluoromethylnaphthalene-2-yl		group,
	7-trifluoromethylnaphthalene-2-yl		group,
	5,6-difluoronaphthalene-2-yl		group,
	5,6-dichloronaphthalene-2-yl		group,
	5,6-dimethylnaphthalene-2-yl		group,
10	5-fluoro-6-methylnaphthalene-2-yl		group,
	6-fluoro-5-methylnaphthalene-2-yl		group,
	5-chloro-6-methylnaphthalene-2-yl		group,
	6-chloro-5-methylnaphthalene-2-yl		group,
	6-chloro-5-fluoronaphthalene-2-yl		group,
15	5-chloro-6-fluoronaphthalene-2-yl	group,	
	4-(2-fluorovinyl)phenyl	group,	4-(2-chlorovinyl)phenyl
	4-(2-bromovinyl)phenyl	group,	4-(2,2-difluorovinyl)phenyl
	group,	4-(2,2-dichlorovinyl)phenyl	group,
	4-(2,2-dibromovinyl)phenyl		group,
20	4-(1-methyl-2,2-dichlorovinyl)phenyl		group,
	4-(1-methyl-2,2-dibromovinyl)phenyl		group,
	4-chloroethynylphenyl	group,	4-bromoethynylphenyl
	4-iodoethynylphenyl	group,	4-methoxymethylphenyl
	4-ethoxymethylphenyl	group,	4-propyloxymethylphenyl
25	4-(1-methoxyethyl)phenyl	group,	4-(2-methoxyethyl)phenyl
	4-(2-methoxypropyl)phenyl	group,	4-(2-methoxyisopropyl)phenyl
	group,	4-phenoxyethylphenyl	group,
	group,	4-(2-phenoxyethyl)phenyl	group,

- 4-(1-phenoxypropyl)phenyl group, 4-(3-phenoxypropyl)phenyl group, 4-(4-phenoxybutyl)phenyl group, 4-(hydroxymethyl)phenyl group,  
 4-(1-hydroxyethyl)phenyl group,  
 4-(2-hydroxyethyl)phenyl group, 4-(1-hydroxypropyl)phenyl group,  
 5 4-(1-hydroxybutyl)phenyl group,  
 4-methylsulfonyloxymethyl)phenyl group,  
 4-ethylsulfonyloxymethyl)phenyl group,  
 4-(1-methylsulfonyloxyethyl)phenyl group,  
 4-(2-sulfonyloxyethyl)phenyl group,  
 10 4-(1-methylsulfonyloxypropyl)phenyl group, 4-carbonylphenyl group, 4-methylcarbonylphenyl group, 4-ethylcarbonylphenyl group, 4-propylcarbonylphenyl group, 4-isopropylcarbonylphenyl group,  
 4-methoxyiminomethylphenyl group,  
 4-(1-methoxyiminoethyl)phenyl group,  
 15 4-(1-methoxyiminopropyl)phenyl group,  
 4-(1-methoxyiminobutyl)phenyl group,  
 4-ethoxyiminomethylphenyl group, 4-(1-ethoxyiminoethyl)phenyl group,  
 4-propoxyiminomethylphenyl group,  
 4-(1-isopropoxyiminoethyl)phenyl group,  
 20 4-(butoxyiminomethyl)phenyl group,  
 4-pentyloxyiminomethylphenyl group,  
 4-(1-hexyloxyiminoethyl)phenyl group,  
 4-benzyloxyiminomethylphenyl group,  
 4-(1-benzyloxyiminoethyl)phenyl group,  
 25 4-(1-benzyloxyiminopropyl)phenyl group,  
 4-(1-benzyloxyiminobutyl)phenyl group,  
 4-dimethylaminoiminomethylphenyl group,  
 4-(1-dimethylaminoiminoethyl)phenyl group,

4-diethylaminoiminomethylphenyl group,  
 4-(1-diethylaminoiminoethyl)phenyl group,  
 4-trimethylsilylphenyl group, 4-triethylsilylphenyl group,  
 4-tert-butyl dimethylsilylphenyl group.

5

The present invention is further illustrated in detail with production examples, formulation examples, test examples and other manner, but should not be limited as follows.

At first, the production examples of the compound of the present invention are illustrated as follows.

10

#### Production Example 1

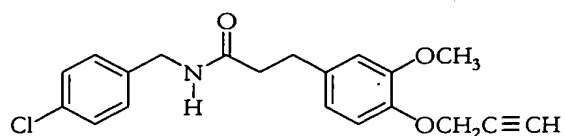
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25

200 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 112 mg of 4-chlorobenzylamine, 0.17 ml of triethylamine and 5 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 212 mg of N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 1 hereinafter).

the compound of the present invention 1

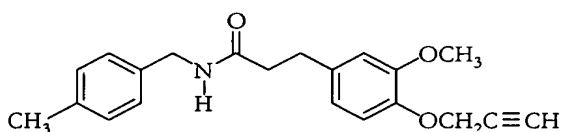


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.25-7.27 (2H, m), 7.05 (2H, d,  $J=8.2$  Hz), 6.94 (1H, d,  $J=8.0$  Hz), 6.71-6.74 (2H, m), 5.59 (1H, br.s), 4.73 (2H, d,  $J=2.5$  Hz), 4.36 (2H, d,  $J=5.9$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.45-2.52 (3H, m)

#### Production Example 2

By using 200 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 99 mg of 4-methylbenzylamine according to the Production Example 1 was obtained 204 mg of N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 2 hereinafter).

the compound of the present invention 2



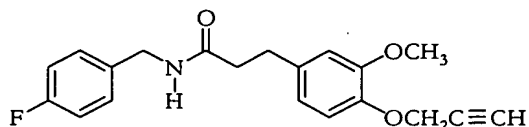
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.11 (2H, d,  $J=8.0$  Hz), 7.05 (2H, d,  $J=8.0$  Hz), 6.94 (1H, d,  $J=8.0$  Hz), 6.71-6.75 (2H, m), 5.53 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.36 (2H, d,  $J=5.5$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.46-2.50 (3H, m), 2.32 (3H, s)

#### Production Example 3

By using 200 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 99 mg of 4-fluorobenzylamine according to the Production Example

1 was obtained 0.13 g of  
 N-(4-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pro  
 panamide (referred as the compound of the present invention 3  
 hereinafter).

5 the compound of the present invention 3

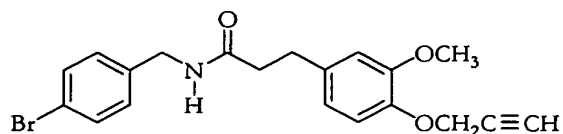


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.09-7.23 (2H, m), 6.93-7.00 (3H,  
 m), 6.71-6.75 (2H, m), 5.57 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz),  
 4.36 (2H, d,  $J=5.8$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz),  
 10 2.48-2.52 (3H, m)

#### Production Example 4

200 mg of  
 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 176  
 mg of 4-bromobenzylamine hydrochloride, 0.29 ml of triethylamine  
 15 and 5 ml of tetrahydrofuran were mixed, and stirred at room  
 temperature for 30 minutes. Then water was added to the reaction  
 mixture, and extracted with ethyl acetate. The organic layer  
 was washed successively with 5 % of hydrochloric acid, saturated  
 aqueous solution of sodium bicarbonate and saturated aqueous  
 20 solution of sodium chloride, dried by magnesium sulfate, and  
 concentrated under reduced pressure. The residue was washed by  
 hexane to obtain 117 mg of  
 N-(4-bromobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}prop  
 anamide (referred as the compound of the present invention 4  
 25 hereinafter).

the compound of the present invention 4

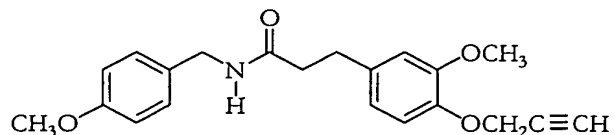


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.41 (2H, d,  $J=8$  Hz), 7.00 (2H, d,  $J=8$  Hz), 6.94 (1H, d,  $J=8.0$  Hz), 6.71-6.74 (2H, m), 5.59 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.34 (2H, d,  $J=5.8$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.49-2.52 (3H, m)

#### Production Example 5

300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-propionyl chloride, 163 mg of 4-methoxybenzylamine, 0.25 ml of triethylamine and 10 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 280 mg of N-(4-methoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 5 hereinafter).

the compound of the present invention 5



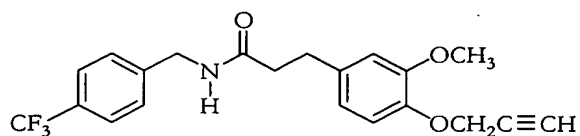
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.08 (2H, d,  $J=8.5$  Hz), 6.93 (1H, d,  $J=8.0$  Hz), 6.83 (2H, d,  $J=8.5$  Hz), 6.71-6.74 (2H, m), 5.54

(1H, br.s), 4.74 (2H, d, J=2.5 Hz), 4.33 (2H, d, J=5.6 Hz), 3.82 (3H, s), 3.79 (3H, s), 2.94 (2H, t, J=7.8 Hz), 2.46-2.49 (3H, m)

#### Production Example 6

5 By using 300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 208 mg of 4-(trifluoromethyl)benzylamine according to the Production Example 5 was obtained 208 mg of N-((4-trifluoromethyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 6 hereinafter).

the compound of the present invention 6



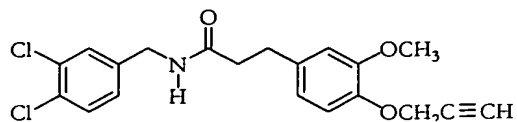
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.54 (2H, d, J=8.0 Hz), 7.23 (1H, d, J=8.2 Hz), 6.94 (2H, d, J=8.0 Hz), 6.71-6.75 (2H, m), 5.68 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.51 (2H, d, J=6.1 Hz), 3.81 (3H, s), 2.96 (2H, t, J=7 Hz), 2.53 (2H, t, J=7 Hz), 2.49 (2H, t, J=2.4 Hz)

#### Production Example 7

20 By using 300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 209 mg of 3,4-dichlorobenzylamine according to the Production Example 5 was obtained 430 mg of N-(3,4-difluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 7 hereinafter).



the compound of the present invention 7

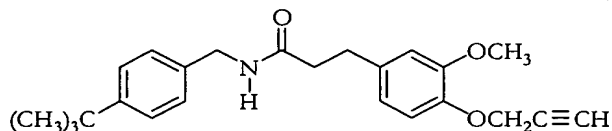


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.35 (1H, d, J=8.2 Hz), 7.28 (1H, d, J=1.9 Hz), 6.93-6.99 (2H, m), 6.71-6.74 (2H, m), 5.64 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.34 (2H, d, J=6.1 Hz), 3.83 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.48-2.54 (3H, m)

Production Example 8

By using 300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 194 mg of 4-tert-butylbenzylamine according to the Production Example 5 was obtained 511 mg of N-(4-tert-butylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 8 hereinafter).

15 the compound of the present invention 8



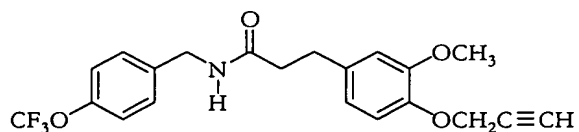
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.33 (2H, d, J=8.5 Hz), 7.10 (2H, d, J=8.5 Hz), 6.94 (1H, d, J=8.0 Hz), 6.71-6.75 (2H, m), 5.67 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.37 (2H, d, J=5.8 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.46-2.50 (3H, m), 1.30 (9H, s)

Production Example 9

By using 300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and

227 mg of 4-(trifluoromethoxy)benzylamine according to the  
 Production Example 5 was obtained 209 mg of  
 N-{4-(trifluoromethoxy)benzyl}-3-{3-methoxy-4-(2-propynyloxy)  
 phenyl}propanamide (referred as the compound of the present  
 5 invention 9 hereinafter).

the compound of the present invention 9

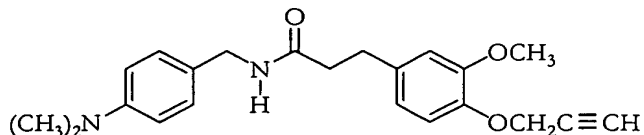


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.12-7.17 (4H, m), 6.95 (1H, d,  $J=8.0$   
 Hz), 6.71-6.76 (2H, m), 5.63 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz),  
 10 4.40 (2H, d,  $J=5.9$  Hz), 3.83 (3H, s), 2.95 (2H, t,  $J=7.6$  Hz),  
 2.48-2.53 (3H, m)

Production Example 10

By using 0.20 g of  
 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.27  
 15 g of 4-dimethylaminobenzylamine hydrochloride and 0.28 ml of  
 triethylamine according to the Production Example 5 was obtained  
 0.40 g of  
 N-(4-dimethylaminobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phe  
 nyl}propanamide (referred as the compound of the present  
 20 invention 10 hereinafter).

the compound of the present invention 10



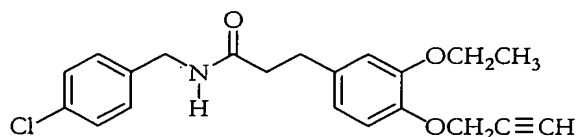
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.03-7.06 (2H, m), 6.93 (1H, d,  $J=8.0$   
 Hz), 6.65-6.76 (4H, m), 5.46 (1H, br.s), 4.72 (2H, d,  $J=2.4$  Hz),

4.29 (2H, d, J=5.5 Hz), 3.83 (3H, s), 2.89-2.95 (8H, m), 2.43-2.49 (3H, m)

#### Production Example 11

0.81 g of 3-(3-ethoxy-4-(2-propynyloxy)phenyl)propionyl  
 5 chloride, 0.46 g of 4-chlorobenzylamine, 0.64 ml of triethylamine  
 and 10 ml of tetrahydrofuran were mixed, and stirred at room  
 temperature for 20 minutes. Then water was added to the reaction  
 mixture, and extracted with ethyl acetate. The organic layer  
 was washed successively with 5 % of hydrochloric acid, saturated  
 10 aqueous solution of sodium bicarbonate and saturated aqueous  
 solution of sodium chloride, dried by magnesium sulfate, and  
 concentrated under reduced pressure. The residue was purified  
 by silica gel column to obtain 0.79 g of  
 N-(4-chlorobenzyl)-3-(3-ethoxy-4-(2-propynyloxy)phenyl)prop  
 15 anamide (referred as the compound of the present invention 11  
 hereinafter).

the compound of the present invention 11



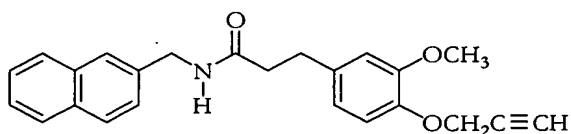
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.24-7.26 (2H, m), 7.04-7.06 (2H,  
 20 m), 6.95 (1H, d, J=8.0 Hz), 6.70-6.74 (2H, m), 5.60 (1H, br.s),  
 4.74 (2H, d, J=2.4 Hz), 4.35 (2H, d, J=5.8 Hz), 4.02 (2H, q,  
 J=7 Hz), 2.92 (2H, t, J=7.5 Hz), 2.27-2.51 (3H, m), 1.42 (3H,  
 t, J=7 Hz)

#### Production Example 12

25 By using 0.30 g of  
 3-(3-methoxy-4-(2-propynyloxy)phenyl)propionyl chloride, 0.19

g of (naphthalene-2-yl)methylamine and 0.5ml of triethylamine according to the Production Example 11 was obtained 0.25 g of N-((naphthalene-2-yl)methyl)-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide (referred as the compound of the present invention 12 hereinafter).

the compound of the present invention 12

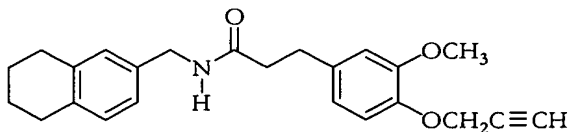


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.76-7.82 (3H, m), 7.60 (1H, s), 7.44-7.49 (2H, m), 7.29-7.29 (1H, m), 6.89-6.90 (1H, m), 6.71-6.95 (2H, m), 5.74 (1H, br.s), 4.69 (2H, d,  $J=2.2$  Hz), 4.55 (2H, d,  $J=5.9$  Hz), 3.78 (3H, s), 2.96 (2H, t,  $J=7.6$  Hz), 2.46-2.54 (3H, m)

Production Example 13

By using 0.30 g of 3-(3-methoxy-4-(2-propynyloxy)phenyl)propionyl chloride, 0.23 g of (5,6,7,8-tetrahydronaphthalene-2-yl)methylamine hydrochloride and 0.42ml of triethylamine according to the Production Example 11 was obtained 0.41 g of N-((5,6,7,8-tetrahydronaphthalene-2-yl)methyl)-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide (referred as the compound of the present invention 13 hereinafter).

the compound of the present invention 13



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.89-7.02 (4H, m), 6.71-6.76 (2H,

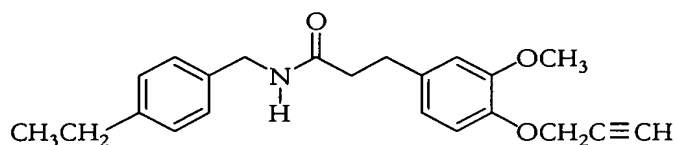
m), 5.52 (1H, br.s), 4.73 (2H, d, J=2.5 Hz), 4.33 (2H, d, J=5.4 Hz), 3.83 (3H, s), 2.92 (2H, t, J=7.8 Hz), 2.49-2.72 (4H, m), 2.45-2.49 (3H, m), 1.76-1.79 (4H, m)

#### Production Example 14

5 By using 0.30 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.16 g of 4-ethylbenzylamine according to the Production Example 5 was obtained 0.40 g of N-(4-ethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}prop

10 anamide (referred as the compound of the present invention 14 hereinafter).

the compound of the present invention 14



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.08-7.15 (4H, m), 6.94 (1H, d, J=8.1 Hz), 6.72-6.75 (2H, m), 5.55 (1H, br.s), 4.73 (2H, d, J=2.2 Hz), 4.37 (2H, d, J=5.6 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.3 Hz), 2.63 (2H, q, J=7 Hz), 2.47-2.50 (3H, m), 1.22 (3H, t, J=7 Hz)

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#### Production Example 15

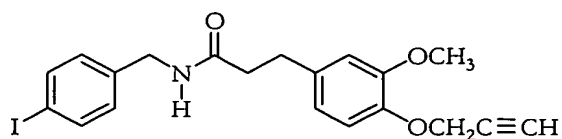
1.1 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl

20 chloride, 1.0 g of 4-iodobenzylamine, 0.98 ml of triethylamine and 20 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated

25 aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and

concentrated under reduced pressure. The residue was washed by hexane to obtain 1.5 g of N-(4-iodobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionamide (referred as the compound of the present invention 15 hereinafter).

the compound of the present invention 15

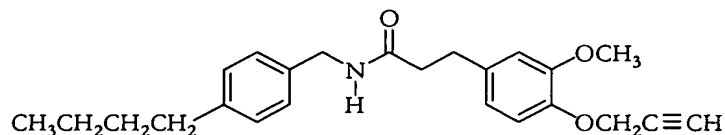


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.60-7.62 (2H, m), 6.93 (1H, d,  $J=8.0$  Hz), 6.86-6.89 (2H, m), 6.70-6.74 (2H, m), 5.61 (1H, br.s), 4.77 (2H, d,  $J=2.5$  Hz), 4.32 (2H, d,  $J=6.1$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.2$  Hz), 2.48-2.52 (3H, m)

Production Example 16

0.50 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.32 g of 4-butylbenzylamine, 0.41 ml of triethylamine and 15 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.60 g of N-(4-butylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionamide (referred as the compound of the present invention 16 hereinafter).

the compound of the present invention 16

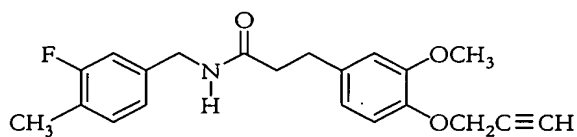


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.06-7.12 (4H, m), 6.94 (1H, d,  $J=8.2$  Hz), 6.71-6.75 (2H, m), 5.59 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz),  
 5 4.36 (2H, d,  $J=5.5$  Hz), 3.82 (3H, s), 2.95 (2H, t,  $J=7.5$  Hz),  
 2.58 (2H, t,  $J=7.5$  Hz), 2.46-2.50 (3H, m), 2.46-2.50 (3H, m),  
 1.53-1.61 (2H, m), 1.30-1.39 (2H, m), 0.92 (3H, t,  $J=7.3$  Hz)

Production Example 17

By using 0.30 g of  
 10 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.17  
 g of 3-fluoro-4-methylbenzylamine and 0.25ml of triethylamine  
 according to the Production Example 11 was obtained 0.34 g of  
 N-(3-fluoro-4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)p  
 henyl}propanamide (referred as the compound of the present  
 15 invention 17 hereinafter).

the compound of the present invention 17



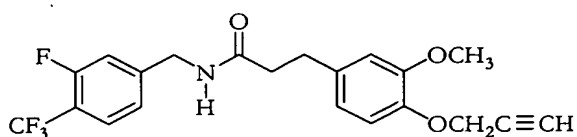
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.09 (1H, t,  $J=7.8$  Hz), 6.94 (1H,  
 d,  $J=8.0$  Hz), 6.70-6.83 (4H, m), 5.58 (1H, br.s), 4.73 (2H, d,  
 20  $J=2.2$  Hz), 4.35 (2H, d,  $J=5.8$  Hz), 3.83 (3H, s), 2.95 (2H, t,  
 $J=7.2$  Hz), 2.48-2.53 (3H, m), 2.24 (3H, s)

Production Example 18

0.50 g of  
 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.50

g of 3-fluoro-4-(trifluoromethyl)benzylamine, 0.41 ml of triethylamine and 10 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.73 g of N-{3-fluoro-4-(trifluoromethyl)benzyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 18 hereinafter).

the compound of the present invention 18



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.51 (1H, t, J=7.7 Hz), 6.94-7.01 (3H, m), 6.72-6.74 (2H, m), 5.71 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.43 (2H, d, J=6.3 Hz), 3.83 (3H, s), 2.96 (2H, t, J=7.5 Hz), 2.55 (2H, t, J=7.5 Hz), 2.48 (1H, t, J=2.4 Hz)

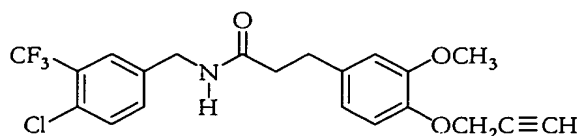
Production Example 19

By using 0.5 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.42 g of 4-chloro-3-(trifluoromethyl)benzylamine and 0.42 ml of triethylamine according to the Production Example 18 was obtained 0.76 g of N-{4-chloro-3-(trifluoromethyl)benzyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the



present invention 19 hereinafter).

the compound of the present invention 19

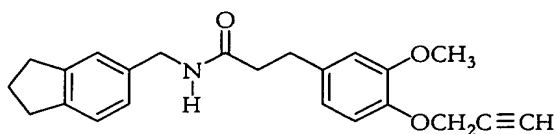


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.53 (1H, d, J=2.2 Hz), 7.42 (1H, d, J=8.2 Hz), 7.20-7.22 (1H, m), 6.94 (1H, d, J=7.8 Hz), 6.71-6.74 (2H, m), 5.69 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.41 (2H, d, J=5.8 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.53 (2H, t, J=7.6 Hz), 2.49 (2H, t, J=2.4 Hz)

Production Example 20

0.50 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.36 g of (indane-5-yl)methylamine hydrochloride, 0.8 ml of triethylamine and 20 ml of tetrahydrofuran were mixed, and stirred at room temperature for 20 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.34 g of N-{(indane-5-yl)methyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 20 hereinafter).

the compound of the present invention 20



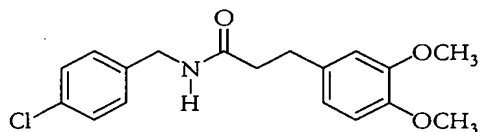
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.71-7.16 (6H, m), 5.54 (1H, br.s), 4.72 (2H, m), 4.36 (2H, d,  $J=4.6$  Hz), 3.82 (3H, s), 2.65-2.94 (6H, m), 2.48 (3H, m), 2.04-2.08 (2H, m)

#### 5 Production Example 21

By using 0.30 g of 3-(3,4-dimethoxyphenyl)propionyl chloride and 0.19 g of 4-chlorobenzylamine according to the Production Example 5 was obtained 0.32 g of N-(4-chlorobenzyl)-3-(3,4-dimethoxyphenyl)propanamide

10 (referred as the compound of the present invention 21 hereinafter).

the compound of the present invention 21



15  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.24-7.27 (2H, m), 7.05-7.07 (2H, m), 6.70-6.77 (3H, m), 5.61 (1H, br.s), 4.36 (2H, d,  $J=5.9$  Hz), 3.86 (3H, s), 3.84 (3H, s), 2.94 (2H, t,  $J=7.6$  Hz), 2.50 (2H, t,  $J=7.6$  Hz)

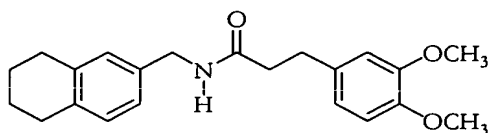
#### Production Example 22

0.30 g of 3-(3,4-dimethoxyphenyl)propionyl chloride, 0.25 g of C-(5,6,7,8-tetrahydronaphthalene-2-yl)methylamine hydrochloride, 0.40 ml of triethylamine and 10 ml of tetrahydrofuran were mixed, and stirred at room temperature for 20 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed

successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to

5 obtain 0.35 g of N-{(5,6,7,8-tetrahydronaphthalene-2-yl)methyl}-3-(3,4-dimethoxyphenyl)propanamide (referred as the compound of the present invention 22 hereinafter).

the compound of the present invention 22



10

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.00 (1H, d, J=8.3 Hz), 6.89 (2H, m), 6.72-6.79 (3H, m), 5.51 (1H, br.s), 4.33 (2H, d, J=5.4 Hz), 3.85 (3H, s), 3.84 (3H, s), 2.94 (2H, t, J=7.6 Hz), 2.73 (4H, m), 2.47 (2H, t, J=7.6 Hz), 1.78 (4H, m)

15 Production Example 23

300 mg of

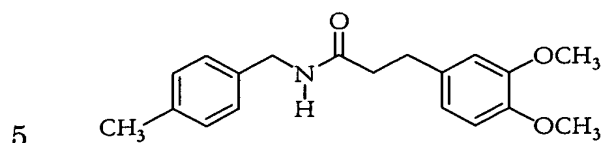
N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide, 0.075ml g of methyl iodide, 0.21 g of potassium carbonate and 5 ml of N,N-dimethylformamide were mixed, and stirred at room temperature for 6 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 226 mg of

25

N-(4-methylbenzyl)-3-(3,4-dimethoxyphenyl)propanamide

(referred as the compound of the present invention 23 hereinafter).

the compound of the present invention 23



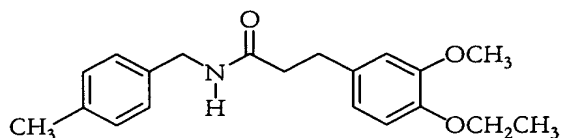
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.10 (2H, d,  $J=8.0$  Hz), 7.05 (2H, d,  $J=8.0$  Hz), 6.70-6.78 (3H, m), 5.53 (1H, br.s), 4.35 (2H, d,  $J=5.6$  Hz), 3.85 (3H, s), 3.83 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.48 (2H, t,  $J=7.7$  Hz), 2.32 (3H, s)

10 Production Example 24

By using 300 mg of N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide and 0.1 ml of ethyl iodide according to the Production Example 23 was obtained 225 mg of

15 N-(4-methylbenzyl)-3-(4-ethoxy-3-methoxyphenyl)propanamide (referred as the compound of the present invention 24 hereinafter).

the compound of the present invention 24

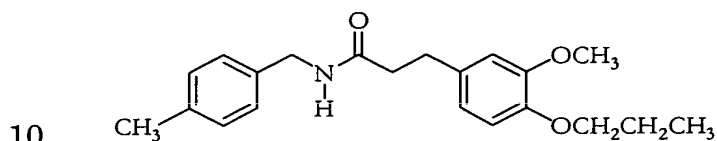


20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.10 (2H, d,  $J=8.0$  Hz), 7.05 (2H, d,  $J=8.0$  Hz), 6.68-6.78 (3H, m), 5.53 (1H, br.s), 4.35 (2H, d,  $J=5.5$  Hz), 4.07 (2H, q,  $J=7.0$  Hz), 3.80 (3H, s), 2.93 (2H, t,  $J=7.5$  Hz), 2.48 (2H, t,  $J=7.7$  Hz), 2.32 (3H, s), 1.45 (2H, t,  $J=7.0$  Hz)

## Production Example 25

By using 300 mg of  
 N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide  
 and 0.12 ml of propyl iodide according to the Production Example  
 5 23 was obtained 262 mg of  
 N-(4-methylbenzyl)-3-(3-methoxy-4-propoxyphenyl)propanamide  
 (referred as the compound of the present invention 25  
 hereinafter).

the compound of the present invention 25



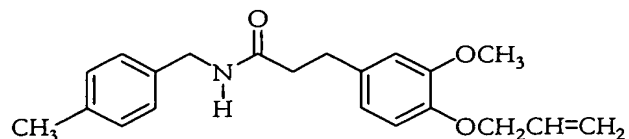
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.11 (2H, d, J=8.1 Hz), 7.05 (2H,  
 d, J=8.0 Hz), 6.69-6.78 (3H, m), 5.54 (1H, br.s), 4.35 (2H, d,  
 J=5.6 Hz), 3.95 (2H, t, J=6.8 Hz), 3.83 (3H, s), 2.93 (2H, t,  
 J=7.6 Hz), 2.48 (2H, t, J=7.6 Hz), 2.32 (3H, s), 1.83-1.89 (2H,  
 15 m) 1.03 (2H, t, J=7.6 Hz)

## Production Example 26

300 mg of  
 N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide,  
 0.104 ml g of allyl bromide, 0.21 g of potassium carbonate and  
 20 5 ml of N,N-dimethylformamide were mixed, and stirred at 60 °C  
 for 6 hours. Then water was added to the reaction mixture, and  
 extracted with ethyl acetate. The organic layer was washed  
 successively with 5 % of hydrochloric acid, saturated aqueous  
 solution of sodium bicarbonate and saturated aqueous solution  
 25 of sodium chloride, dried by magnesium sulfate, and concentrated  
 under reduced pressure. The residue was washed by hexane to

obtain 366 mg of  
 N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propenyloxy)phenyl}propanamide (referred as the compound of the present invention 26 hereinafter).

5 the compound of the present invention 26

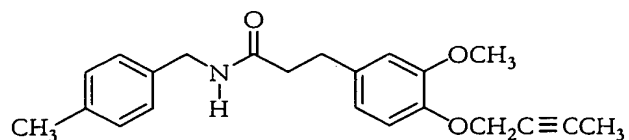


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.10 (2H, d, J=8.0 Hz), 7.05 (2H, d, J=8.0 Hz), 6.68-6.83 (3H, m), 6.02-6.12 (1H, m), 5.54 (1H, br.s), 5.39 (2H, d, J=17.2 Hz), 5.27 (2H, d, J=10.5 Hz), 4.57  
 10 (2H, d, J=5.3 Hz), 4.35 (2H, d, J=5.5 Hz), 3.82 (3H, s), 2.93 (2H, t, J=7.8 Hz), 2.47 (2H, t, J=7.8 Hz), 2.32 (3H, s)

Production Example 27

By using 0.30 g of  
 N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide  
 15 and 0.11 ml of 1-bromo-2-butyne according to the Production  
 Example 23 was obtained 0.31 g of  
 N-(4-methylbenzyl)-3-{3-methoxy-4-(2-butynyloxy)phenyl}propanamide (referred as the compound of the present invention 27 hereinafter).

20 the compound of the present invention 27

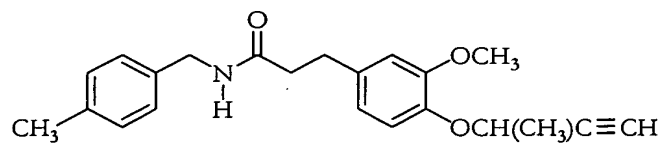


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.04-7.12 (4H, m), 6.92 (1H, d, J=7.8 Hz), 6.71-6.73 (2H, m), 5.53 (1H, br.s), 4.68 (2H, d, J=2.2 Hz), 4.36 (2H, d, J=5.6 Hz), 3.82 (3H, s), 2.94 (2H, t, J=7.8 Hz),

2.48 (2H, t, J=7.8 Hz), 2.33 (3H, s), 1.84 (3H, t, J=2.2 Hz)

# Production Example 28

0.11 g of 1-methyl-2-propynol, 0.11 ml of methanesulfonyl chloride, 0.28 ml of triethylamine and 3 ml of tetrahydrofuran were mixed, and stirred at room temperature for 30 minutes. Then ethyl acetate was added to the reaction mixture, and filtered. The filtrate was concentrated under reduced pressure. The obtained residue, 0.30 g of N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide 0.21 g of potassium carbonate and 5 ml of N,N-dimethylformamide were mixed, and stirred at 60 °C for 6 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 0.16 g of N-(4-methylbenzyl)-3-{3-methoxy-4-(1-methyl-2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 28 hereinafter).

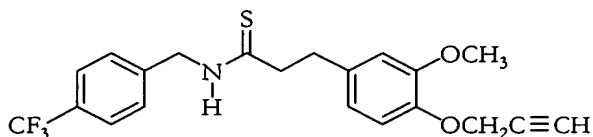


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.98-7.12 (4H, m), 6.82 (1H, d, J=7.8 Hz), 6.66-6.74 (2H, m), 5.54 (1H, br.s), 4.84-4.87 (1H, m), 4.35 (2H, d, J=5.5 Hz), 3.83 (3H, s), 2.92 (2H, t, J=7.2 Hz), 2.43-2.50 (2H, m), 2.32 (3H, s), 2.17 (3H, s), 1.69 (1H, d, J=6.6 Hz)

## Production Example 29

1.4 g of  
 N-(4-trifluoromethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 1.6 g of Lawesson's Reagent and 20 ml of tetrahydrofuran were mixed, and stirred at 65 °C for 3 hours. Then the reaction mixture was cooled, water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 3 % of aqueous solution of sodium hydroxide, 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 1.3 g of N-(4-trifluoromethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 29 hereinafter).

the compound of the present invention 29



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.56 (2H, d, J=8 Hz), 7.19 (2H, d, J=8 Hz), 7.12 (1H, br.s), 6.93 (1H, d, J=8.2 Hz), 6.72-6.76 (2H, m), 4.81 (2H, d, J=5.3 Hz), 4.73 (2H, d, J=2.4 Hz), 3.81 (3H, s), 3.11 (2H, t, J=6.8 Hz), 2.97 (2H, t, J=6.8 Hz), 2.47 (1H, t, J=2.4 Hz)

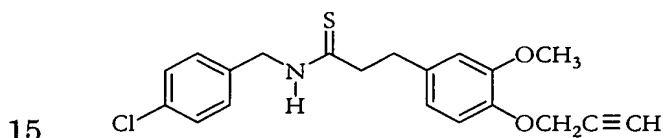
## Production Example 30

0.59 g of  
 N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pr



5 opanamide, 0.67 g of Lawesson's Reagent and 10 ml of  
 tetrahydrofuran were mixed, and stirred at 65 °C for 3 hours.  
 Then the reaction mixture was cooled, and concentrated under  
 reduced pressure. Water was added to the residue and extracted  
 with ethyl acetate. The organic layer was washed successively  
 with 3 % of aqueous solution of sodium hydroxide, 5 % hydrochloric  
 acid, saturated aqueous solution of sodium bicarbonate and  
 saturated aqueous solution of sodium chloride, dried by magnesium  
 sulfate, and concentrated under reduced pressure. The residue  
 10 was purified by silica gel column to obtain 0.59 g of  
 N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pro-  
 panthioamide (referred as the compound of the present invention  
 30 hereinafter).

the compound of the present invention 30



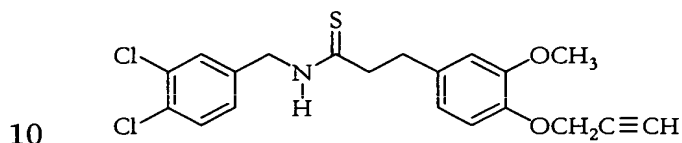
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.26-7.29 (2H, m), 6.99-7.06 (3H,  
 m), 6.92 (1H, d, J=8.0 Hz), 6.70-6.75 (2H, m), 4.73 (2H, d, J=2  
 Hz), 4.70 (2H, d, J=5.3 Hz), 3.82 (3H, s), 3.09 (2H, t, J=7.2  
 Hz), 2.97 (2H, t, J=7.2 Hz), 2.49 (1H, t, J=2 Hz)

## 20 Production Example 31

0.40 g of  
 N-(3,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.45 g of Lawesson's Reagent and 15 ml of  
 tetrahydrofuran were mixed, and stirred at 65 °C for 3 hours.  
 25 Then the reaction mixture was cooled. Water was added to the  
 reaction mixture and extracted with ethyl acetate. The organic

layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was  
 5 purified by silica gel column to obtain 0.42 g of N-(3,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 31 hereinafter).

the compound of the present invention 31



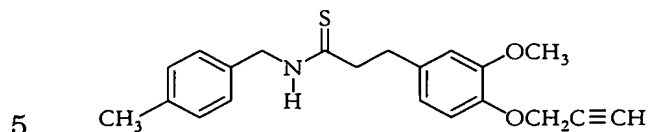
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.34 (1H, d,  $J=8.2$  Hz), 7.28 (1H, d,  $J=2.2$  Hz), 7.12 (1H, br.s), 6.89-6.99 (2H, m), 6.71-6.75 (2H, m), 4.70-4.73 (4H, m), 3.82 (3H, s), 3.09 (2H, t,  $J=7.5$  Hz), 2.96 (2H, t,  $J=7.5$  Hz), 2.49 (1H, t,  $J=2.1$  Hz)

15 Production Example 32

0.40 g of N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.53 g of Lawesson's Reagent and 10 ml of tetrahydrofuran were mixed, and stirred at 65 °C for 3 hours. Then the reaction  
 20 mixture was cooled, and concentrated under reduced pressure. Water was added to the residue and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium  
 25 sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 0.38 g of

N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 32 hereinafter).

the compound of the present invention 32



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.12 (2H, d,  $J=7.8$  Hz), 6.91-7.02 (3H, m), 6.92 (1H, d,  $J=8.2$  Hz), 6.75 (1H, d,  $J=1.9$  Hz), 6.72 (1H, dd,  $J=8.2$  Hz, 1.9 Hz), 4.72 (2H, d,  $J=2$  Hz), 4.66 (2H, d,  $J=4.8$  Hz), 3.82 (3H, s), 3.08 (2H, t,  $J=7.2$  Hz), 2.97 (2H, t,  $J=7.2$  Hz), 2.48 (1H, t,  $J=2$  Hz), 2.33 (3H, s)

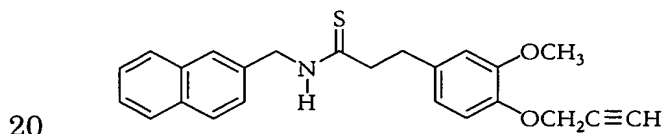
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Production Example 33

By using 0.61 g of N-((naphthalene-2-yl)methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 745 mg of Lawesson's Reagent according to the Production Example 32 was obtained 0.38 g of N-((naphthalene-2-yl)methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 33 hereinafter).

15

the compound of the present invention 33



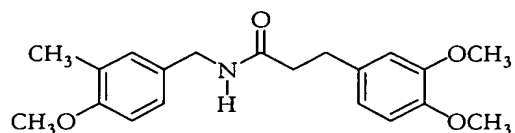
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.7-8.9 (3H, m), 7.60 (1H, s), 7.4-7.6 (2H, m), 7.20 (1H, dd,  $J=8.5$  Hz, 1.7 Hz), 7.15 (1H, br), 6.88 (1H, d,  $J=8.0$  Hz), 6.77 (1H, d,  $J=1.9$  Hz), 6.72 (1H, dd,  $J=8.2$  Hz, 1.8 Hz), 4.88 (2H, d,  $J=5.1$  Hz), 4.67 (2H, d,  $J=2.4$  Hz),

3.80 (3H, s), 3.10 (2H, t, J=7.2 Hz), 2.96 (2H, t, J=7.2 Hz),  
2.44 (1H, t, J=2.4 Hz)

#### Production Example 34

By using 686 mg of 3-(3,4-dimethoxyphenyl)propionyl  
5 chloride, 563 mg of 4-methoxy-3-methylbenzylamine hydrochloride  
and 758 mg of triethylamine according to the Production Example  
4 was obtained 900 mg of  
N-(4-methoxy-3-methylbenzyl)-3-(3,4-dimethoxyphenyl)propana  
mide (referred as the compound of the present invention 34  
10 hereinafter).

the compound of the present invention 34

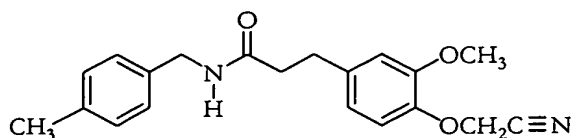


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.9-7.0 (2H, m), 6.7-6.8 (4H, m),  
5.49 (1H, br), 4.30 (2H, d, J=5.6 Hz), 3.84 (3H, s), 3.83 (3H,  
15 s), 3.80 (3H, s), 2.93 (2H, t, J=7.5 Hz), 2.46 (2H, t, J=7.6  
Hz), 2.18 (3H, s)

#### Production Example 35

By using 0.30 g of  
N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide  
20 and 0.08 ml of chloroacetonitrile according to the Production  
Example 23 was obtained 0.19 g of  
N-(4-methylbenzyl)-3-{3-methoxy-4-cyanomethoxyphenyl}propan  
amide (referred as the compound of the present invention 35  
hereinafter).

25 the compound of the present invention 35

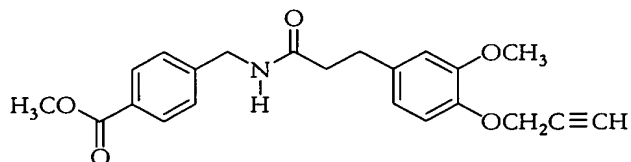


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.09-7.12 (4H, m), 6.96 (1H, d, J=8.2 Hz), 6.73-6.80 (2H, m), 5.59 (1H, br.s), 4.78 (2H, s), 4.47 (2H, d, J=5.5 Hz), 3.83 (3H, s), 2.96 (2H, t, J=7.3 Hz), 2.48 (2H, t)

#### Production Example 36

By using 1.0 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.90 g of 4-methoxycarbonylbenzylamine hydrochloride according to the Production Example 18 was obtained 0.82 g of N-(4-methoxycarbonylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 36 hereinafter).

the compound of the present invention 36



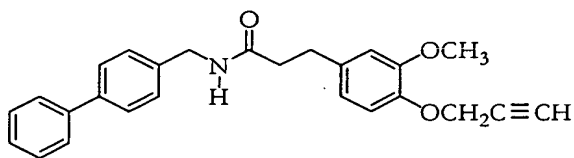
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.94-7.97 (2H, m), 7.12-7.21 (2H, m), 6.94 (1H, d, J=8.0 Hz), 6.71-6.75 (2H, m), 5.48 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.46 (2H, d, J=6.0 Hz), 3.91 (3H, s), 3.82 (3H, s), 2.96 (2H, t, J=7.2 Hz), 2.47-2.55 (3H, m)

#### 20 Production Example 37

884 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 641 mg of 4-phenylbenzylamine, 530 mg of triethylamine and 10 ml tetrahydrofuran were mixed, and stirred at room temperature for

1 hour. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 1.00 g of N-(4-phenylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 37 hereinafter).

10 the compound of the present invention 37



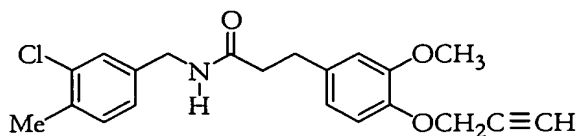
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.50-7.60 (4H, m), 7.40-7.47 (2H, m), 7.31-7.38 (1H, m), 7.22 (2H, d, J=8.3 Hz), 6.94 (1H, d, J=7.8 Hz), 6.71-6.77 (2H, m), 5.63 (1H, br.s), 4.72 (2H, d, J=2.2 Hz), 4.44 (2H, d, J=5.8 Hz), 3.81 (3H, s), 2.96 (2H, t, J=7.5 Hz), 2.52 (2H, t, J=7.5 Hz), 2.45 (1H, t, J=2.4 Hz)

#### Production Example 38

In the same way as in the Production Example 37, 100 mg of

20 N-(3-chloro-4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 38 hereinafter) was obtained from 884 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 554 mg of 3-chloro-4-methyl-benzylamine.

25 the compound of the present invention 38

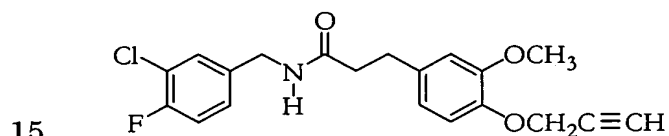


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.18 (1H, d, J=1.7 Hz), 7.14 (1H, d, J=7.7 Hz), 6.91-6.96 (2H, m), 6.70-6.75 (2H, m), 4.73 (2H, d, J=2.4 Hz), 5.57 (1H, br.s), 4.34 (2H, d, J=5.8 Hz), 3.82 (3H, s), 2.94 (2H, t, J=7.5 Hz), 2.45-2.53 (3H, m), 2.34 (3H, s)

Production Example 39

In the same way as in the Production Example 37, 1.03 g of N-(3-chloro-4-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 39 hereinafter) was obtained from 884 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 559 mg of 3-chloro-4-fluorobenzylamine.

the compound of the present invention 39



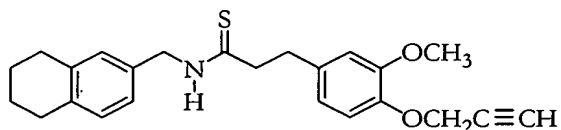
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.21-7.26 (2H, m), 6.92-7.10 (3H, m), 6.70-6.76 (2H, m), 5.63 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.34 (2H, d, J=5.8 Hz), 3.83 (3H, s), 2.95 (2H, t, J=7.3 Hz), 2.51 (2H, t, J=7.3 Hz), 2.48 (1H, t, J=2.2 Hz)

Production Example 40

637 mg of N-(5,6,7,8-tetrahydronaphthalen-2-ylmethyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 769 mg of Lawesson's Reagent and 10 ml of tetrahydrofuran were mixed, and stirred

at 65 °C for 3 hours. Then the reaction mixture was cooled, and concentrated under reduced pressure. Water was added to the residue and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 394 mg of N-(5,6,7,8-tetrahydronaphthalene-2-ylmethyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 40 hereinafter).

the compound of the present invention 40



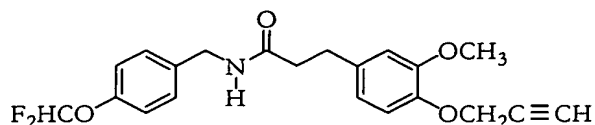
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.91-7.03 (3H, m), 6.85 (2H, d, J=7.5 Hz), 6.76 (1H, d, J=2.0 Hz), 6.72 (1H, dd, J=8.1 Hz, 2.0 Hz), 4.72 (2H, d, J=2.2 Hz), 4.62 (2H, d, J=4.6 Hz), 3.82 (3H, s), 3.08 (2H, t, J=7.3 Hz), 2.91 (2H, t, J=7.3 Hz), 2.69-2.77 (4H, m), 2.48 (1H, t, J=2.4 Hz), 1.75-1.81 (4H, m)

#### Production Example 41

In the same way as in the Production Example 37, 700 mg of N-(4-difluoromethoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 41 hereinafter) was obtained from 884 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 606 mg of 4-difluoromethoxybenzylamine.



the compound of the present invention 41

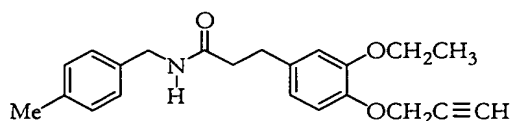


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.12 (2H, d,  $J=8.4$  Hz), 7.03 (2H, d,  $J=8.4$  Hz), 6.93 (1H, d,  $J=7.7$  Hz), 6.70-6.75 (2H, m), 6.49 (1H, t,  $J=73$  Hz), 5.59 (1H, br.s), 4.73 (2H, d,  $J=2.2$  Hz), 4.37 (2H, d,  $J=5.8$  Hz), 3.81 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.46-2.54 (3H, m)

#### Production Example 42

In the same way as in the Production Example 37, 1.02 g of  
 10 of  
 N-(4-methylbenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 42 hereinafter) was obtained from 0.93 g of  
 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionyl chloride and  
 15 0.42 g of 4-methylbenzylamine.

the compound of the present invention 42

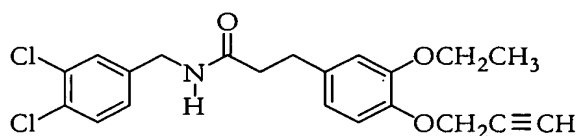


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.03-7.12 (4H, m), 6.94 (1H, d,  $J=8.2$  Hz), 6.74 (1H, d,  $J=1.9$  Hz), 6.70 (1H, dd,  $J=2.1$  Hz, 8.2 Hz),  
 20 5.53 (1H, br.s), 4.72 (2H, d,  $J=2.4$  Hz), 4.35 (2H, d,  $J=5.5$  Hz), 4.03 (2H, q,  $J=7.0$  Hz), 2.92 (2H, t,  $J=7.7$  Hz), 2.45-2.50 (3H, m), 2.32 (3H, s), 1.42 (3H, t,  $J=7.0$  Hz)

#### Production Example 43

In the same way as in the Production Example 37, 1.34 g of  
 25 of

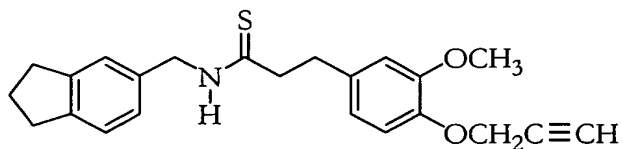
N-(3,4-dichlorobenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl} propanamide (referred as the compound of the present invention 43 hereinafter) was obtained from 0.93 g of 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.62 g of 3,4-dichlorobenzylamine.  
the compound of the present invention 43



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.27-7.37 (2H, m), 6.92-6.98 (2H, m), 6.68-6.75 (2H, m), 5.62 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.34 (2H, d,  $J=6.0$  Hz), 4.03 (2H, q,  $J=7.0$  Hz), 2.93 (2H, t,  $J=7.2$  Hz), 2.45-2.55 (3H, m), 1.42 (3H, t,  $J=7.0$  Hz)

#### Production Example 44

In the same way as in the Production Example 40, 350 mg of N-(indan-5-yl methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 44 hereinafter) was obtained from 500 mg of N-(indan-5-yl methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 627 mg of Lawesson's Reagent.  
the compound of the present invention 44

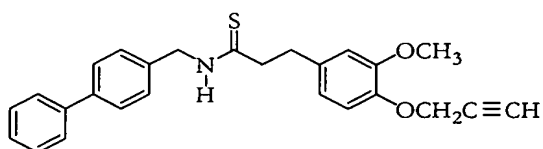


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.16 (1H, d,  $J=7.7$  Hz), 6.86-7.10 (4H, m), 6.75 (1H, d,  $J=1.9$  Hz), 6.72 (1H, dd,  $J=8.2$  Hz, 1.9 Hz), 4.72 (2H, d,  $J=2.4$  Hz), 4.65 (2H, d,  $J=4.8$  Hz), 3.81 (3H,

s), 3.08 (2H, t, J=7.4 Hz), 2.84-2.95 (6H, m), 2.47 (1H, t, J=2.4 Hz), 2.01-2.11 (2H, m)

#### Production Example 45

In the same way as in the Production Example 40, 314 mg  
 5 of  
 N-(4-phenylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention  
 45 hereinafter) was obtained from 500 mg of  
 N-(4-phenylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 571 mg of Lawesson's Reagent.  
 10 the compound of the present invention 45



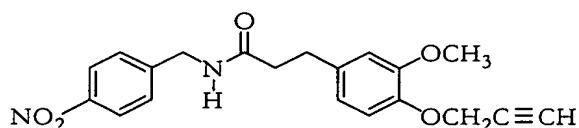
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.52-7.58 (4H, m), 7.40-7.46 (2H, m), 7.33-7.37 (1H, m), 7.15-7.23 (3H, m), 6.92 (1H, d, J=8.1 Hz), 6.71-6.77 (2H, m), 4.76 (2H, d, J=5.1 Hz), 4.70 (2H, d, J=2.4 Hz), 3.79 (3H, s), 3.09 (2H, t, J=7.2 Hz), 2.94 (2H, t, J=7.2 Hz), 2.44 (1H, t, J=2.4 Hz)

#### Production Example 46

0.50 g of 3-{3-methoxy-4-(propynyloxy)phenyl}propionyl  
 20 chloride, 0.39 g of 4-nitrobenzylamine, 0.69 ml triethylamine  
 and 10 ml of tetrahydrofuran were mixed, and stirred at room  
 temperature for 1 hour. Then water was added to the reaction  
 mixture and extracted with ethyl acetate. The organic layer was  
 washed successively with 5% hydrochloric acid, saturated aqueous  
 25 solution of sodium bicarbonate and saturated aqueous solution  
 of sodium chloride, dried by magnesium sulfate, and concentrated

under reduced pressure. The residue was purified by silica gel column to obtain 0.32 g of N-(4-nitrobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 46 hereinafter).

the compound of the present invention 46

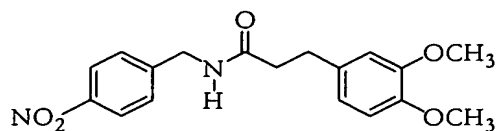


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.12-8.15 (2H, m), 7.25-7.28 (2H, m), 6.96 (1H, d,  $J=7.1$  Hz), 6.72-6.75 (2H, m), 5.72 (1H, br.s), 4.75 (2H, d,  $J=2.4$  Hz), 4.49 (2H, d,  $J=6.3$  Hz), 3.83 (3H, s), 2.96 (2H, t,  $J=7.5$  Hz), 2.56 (2H, t,  $J=7.5$  Hz), 2.50 (1H, t,  $J=2.4$  Hz)

#### Production Example 47

0.50 g of 3-(3,4-dimethoxyphenyl)propionyl chloride, 0.43 g of 4-nitrobenzylamine, 0.71 ml triethylamine and 10 ml of tetrahydrofuran were mixed, and stirred at room temperature for 1 hour. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 0.30 g of N-(4-nitrobenzyl)-3-(3,4-dimethoxyphenyl)propanamide (referred as the compound of the present invention 47 hereinafter).

the compound of the present invention 47



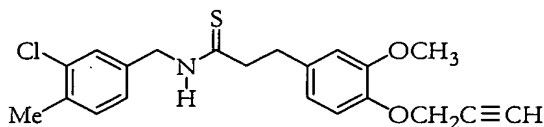
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.10-8.12 (2H, m), 7.24-7.26 (2H, m), 6.73-6.78 (3H, m), 5.78 (1H, br.s), 4.49 (2H, d, J=5.8 Hz),  
 5 3.86 (3H, s), 3.84 (3H, s), 2.96 (2H, t, J=7.2 Hz), 2.55 (2H, t, J=7.2 Hz)

#### Production Example 48

In the same way as in the Production Example 40, 338 mg of

10 N-(3-chloro-4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 48 hereinafter) was obtained from 560 mg of N-(3-chloro-4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 683 mg of Lawesson's Reagent.

15 the compound of the present invention 48



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.13-7.18 (2H, m), 7.05 (1H, br.s), 6.86-6.95 (2H, m), 6.70-6.76 (2H, m), 4.72 (2H, d, J=2.4 Hz), 4.67 (2H, d, J=5.3 Hz), 3.82 (3H, s), 3.08 (2H, t, J=7.0 Hz),  
 20 2.93 (2H, t, J=7.0 Hz), 2.47 (1H, t, J=2.1 Hz), 2.34 (3H, s)

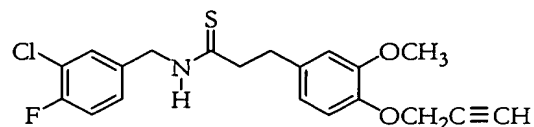
#### Production Example 49

In the same way as in the Production Example 40, 345 mg of

N-(3-chloro-4-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}

henyl}propanthioamide (referred as the compound of the present invention 49 hereinafter) was obtained from 500 mg of N-(3-chloro-4-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)p

5 the compound of the present invention 49



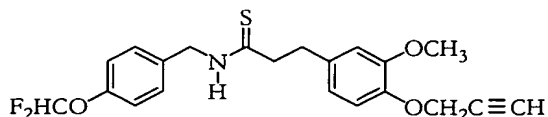
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.23 (1H, dd,  $J=7.0$  Hz, 2.0 Hz), 7.19 (1H, br.s), 7.07 (1H, t,  $J=8.6$  Hz), 6.90-6.97 (2H, m), 6.75 (1H, d,  $J=1.7$  Hz), 6.72 (1H, dd,  $J=8.0$  Hz, 1.9 Hz), 4.72 (2H, d,  $J=2.4$  Hz), 4.70 (2H, d,  $J=5.3$  Hz), 3.81 (3H, s), 3.08 (2H, t,  $J=7.2$  Hz), 2.94 (2H, t,  $J=7.2$  Hz), 2.48 (1H, t,  $J=2.4$  Hz)

Production Example 50

In the same way as in the Production Example 40, 483 mg of

15 N-(4-difluoromethoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)p  
henyl}propanthioamide (referred as the compound of the present invention 50 hereinafter) was obtained from 550 mg of N-(4-difluoromethoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)p

20 the compound of the present invention 50

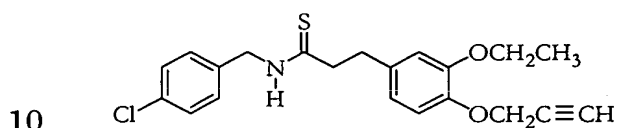


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.24 (1H, br.s), 7.01-7.12 (4H, m), 6.91 (1H, d,  $J=8.0$  Hz), 6.71-6.74 (2H, m), 6.52 (1H, t,  $J=7.4$  Hz), 4.67-4.73 (4H, m), 3.78 (3H, s), 3.07 (2H, t,  $J=7.0$  Hz), 2.93 (2H, t,  $J=7.0$  Hz), 2.48 (1H, t,  $J=2.4$  Hz)

## Production Example 51

In the same way as in the Production Example 40, 360 mg of

5 N-(4-chlorobenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl}prop  
anthioamide (referred as the compound of the present invention  
51 hereinafter) was obtained from 425 mg of  
N-(4-chlorobenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl}prop  
anamide and 330 mg of Lawesson's Reagent.  
the compound of the present invention 51

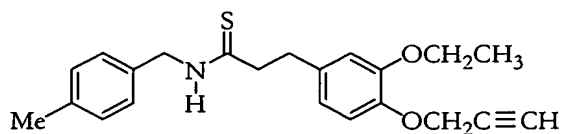


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.41 (1H, br.s), 7.25 (2H, d, J=8.4  
Hz), 7.01 (2H, d, J=8.2 Hz), 6.91 (1H, d, J=8.2 Hz), 6.73 (1H,  
d, J=1.9 Hz), 6.69 (1H, dd, J=8.0 Hz, 1.9 Hz), 4.67-4.71 (4H,  
m), 3.99 (2H, q, J=7.0 Hz), 3.05 (2H, t, J=7.1 Hz), 2.91 (2H,  
15 t, J=7.1 Hz), 2.48 (1H, t, J=2.4 Hz), 1.40 (3H, t, J=6.9 Hz)

## Production Example 52

In the same way as in the Production Example 40, 423 mg of

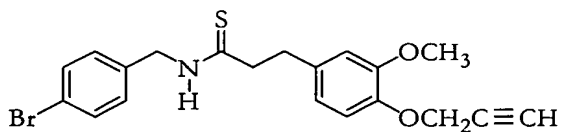
20 N-(4-methylbenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl}prop  
anthioamide (referred as the compound of the present invention  
52 hereinafter) was obtained from 0.53 g of  
N-(4-methylbenzyl)-3-{3-ethoxy-4-(2-propynyloxy)phenyl}prop  
anamide and 0.44 g of Lawesson's Reagent.  
the compound of the present invention 52



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.21 (1H, br.s), 7.10 (2H, d, J=7.7 Hz), 7.00 (2H, d, J=7.9 Hz), 6.91 (1H, d, J=7.9 Hz), 6.74 (1H, d, J=1.9 Hz), 6.69 (1H, dd, J=8.2 Hz, 1.9 Hz), 4.69 (2H, d, J=2.1 Hz), 4.65 (2H, d, J=5.0 Hz), 4.00 (2H, q, J=7.0 Hz), 3.04 (2H, t, J=7.2 Hz), 2.89 (2H, t, J=7.2 Hz), 2.46 (1H, t, J=2.1 Hz), 2.32 (3H, s), 1.40 (3H, t, J=6.7 Hz)

#### Production Example 53

In the same way as in the Production Example 40, 463 mg of  
 10 of  
 N-(4-bromobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 53 hereinafter) was obtained from 660 mg of  
 15 N-(4-bromobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 435 mg of Lawesson's Reagent.  
 the compound of the present invention 53



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.39-7.43 (2H, m), 7.28 (1H, br.s), 6.95 (2H, d, J=8.4 Hz), 6.90 (1H, d, J=8.2 Hz), 6.74 (1H, d, J=1.7 Hz), 6.70 (1H, dd, J=7.9 Hz, 2.0 Hz), 4.71 (2H, d, J=2.4 Hz), 4.68 (2H, d, J=5.3 Hz), 3.79 (3H, s), 3.07 (2H, t, J=7.1 Hz), 2.93 (2H, t, J=7.1 Hz), 2.49 (1H, t, J=2.4 Hz)

#### Production Example 54

In the same way as in the Production Example 40, 360 mg

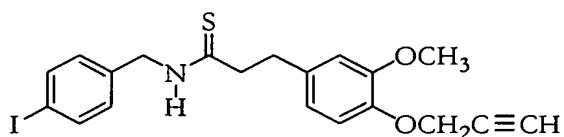


of

N-(4-iodobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 54 hereinafter) was obtained from 541 mg of

5 N-(4-iodobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 348 mg of Lawesson's Reagent.

the compound of the present invention 54



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.63 (2H, d,  $J=7.9$  Hz), 7.03 (1H, br.s), 6.92 (1H, d,  $J=7.9$  Hz), 6.83 (2H, d,  $J=7.7$  Hz), 6.75 (1H, d,  $J=1.9$  Hz), 6.71 (1H, dd,  $J=7.9$  Hz, 1.7 Hz), 4.74 (2H, d,  $J=2.4$  Hz), 4.67 (2H, d,  $J=5.0$  Hz), 3.81 (3H, s), 3.08 (2H, t,  $J=7.1$  Hz), 2.94 (2H, t,  $J=7.1$  Hz), 2.49 (1H, t,  $J=2.4$  Hz)

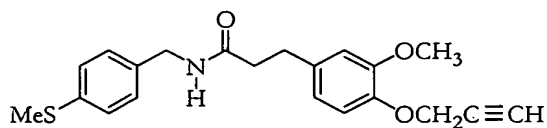
Production Example 55

15 In the same way as in the Production Example 37, 830 mg of

N-(4-methylthiobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 55 hereinafter) was obtained from 632 mg of

20 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 383 mg of 4-methylthiobenzylamine.

the compound of the present invention 55

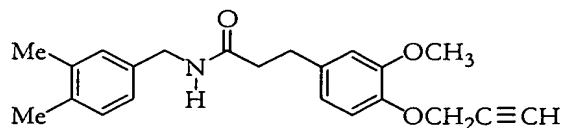


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.18 (2H, d,  $J=8.0$  Hz), 7.06 (2H,

d,  $J=8.2$  Hz), 6.93 (1H, d,  $J=8.0$  Hz), 6.70-6.75 (2H, m), 5.56 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.35 (2H, d,  $J=5.8$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.1$  Hz), 2.45-2.53 (6H, m)

#### Production Example 56

5           In the same way as in the Production Example 37, 830 mg of  
of  
N-(3,4-dimethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}  
}propanamide (referred as the compound of the present invention  
56 hereinafter) was obtained from 632 mg of  
10 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and  
338 mg of 3,4-dimethylbenzylamine.  
the compound of the present invention 56

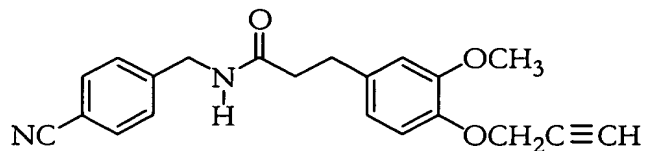


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.06 (1H, d,  $J=7.5$  Hz), 6.88-7.00  
15 (3H, m), 6.75 (1H, d,  $J=1.9$  Hz), 6.73 (1H, dd,  $J=8.0$  Hz, 1.9  
Hz), 5.51 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.34 (2H, d,  $J=5.3$   
Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.3$  Hz), 2.44-2.51 (3H, m),  
2.23 (6H, s)

#### Production Example 57

20           In the same way as in the Production Example 37, 1.44 g of  
of  
N-(4-cyano-benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pro  
panamide (referred as the compound of the present invention 57  
hereinafter) was obtained from 1.61 g of  
25 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and  
0.84 g of 4-cyanobenzylamine.

the compound of the present invention 57

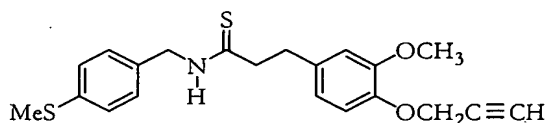


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.56 (2H, d,  $J=7.9$  Hz), 7.18 (2H, d,  $J=7.9$  Hz), 6.95 (1H, d,  $J=7.7$  Hz), 6.71-6.75 (2H, m), 5.71 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.44 (2H, d,  $J=6.0$  Hz), 3.82 (3H, s), 2.95 (2H, t,  $J=7.4$  Hz), 2.54 (2H, t,  $J=7.2$  Hz), 2.50 (1H, t,  $J=2.4$  Hz)

#### Production Example 58

In the same way as in the Production Example 40, 390 mg of  
 10 of  
 N-(4-methylthiobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}  
 }propanthioamide (referred as the compound of the present  
 invention 58 hereinafter) was obtained from 0.52 g of  
 N-(4-methylthiobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}  
 15 }propanamide and 0.41 g of Lawesson's Reagent.

the compound of the present invention 58



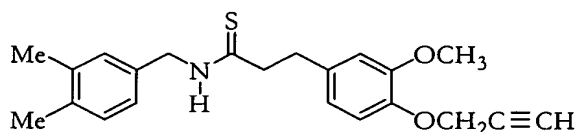
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.18 (1H, d,  $J=8.2$  Hz), 6.99-7.06 (3H, m), 6.91 (1H, d,  $J=8.2$  Hz), 6.75 (1H, d,  $J=1.9$  Hz), 6.71 (1H, dd,  $J=7.9$  Hz, 1.9 Hz), 4.72 (2H, d,  $J=2.1$  Hz), 4.66 (2H, d,  $J=5.0$  Hz), 3.81 (3H, s), 3.08 (2H, t,  $J=7.2$  Hz), 2.93 (2H, t,  $J=7.2$  Hz), 2.49 (1H, t,  $J=2.4$  Hz), 2.47 (3H, s)

#### Production Example 59

In the same way as in the Production Example 40, 345 mg  
 25 of

N-(3,4-dimethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl  
 }propanthioamide) (referred as the compound of the present  
 invention 59 hereinafter) was obtained from 0.43 g of  
 N-(3,4-dimethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl  
 }propanamide and 0.36 g of Lawesson's Reagent.

the compound of the present invention 59



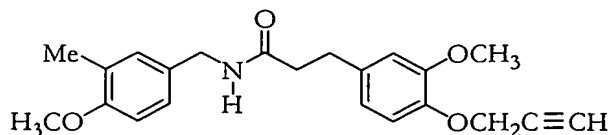
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.08 (1H, d, J=7.8 Hz), 7.01 (1H,  
 br.s), 6.84-6.96 (3H, m), 6.76 (1H, d, J=1.9 Hz), 6.72 (1H, dd,  
 J=8.1 Hz, 1.9 Hz), 4.72 (2H, d, J=2.2 Hz), 4.63 (2H, d, J=4.8  
 Hz), 3.82 (3H, s), 3.08 (2H, t, J=7.3 Hz), 2.91 (2H, t, J=7.3  
 Hz), 2.47 (1H, t, J=2.4 Hz), 2.43 (3H, s), 2.23 (3H, s)

Production Example 60

In the same way as in the Production Example 37, 830 mg  
 of

N-(4-methoxy-3-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)  
 phenyl}propanamide (referred as the compound of the present  
 invention 60 hereinafter) was obtained from 0.76 g of  
 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and  
 0.56 g of 4-methoxy-3-methylbenzylamine hydrochloride.

the compound of the present invention 60

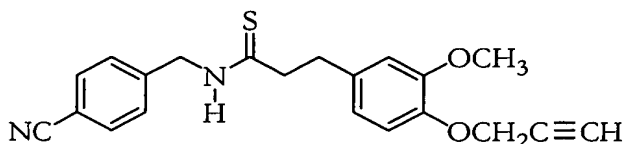


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.91-6.98 (3H, m), 6.70-6.76 (3H,  
 m), 5.49 (1H, br.s), 4.72 (2H, d, J=2.4 Hz), 4.30 (2H, d, J=5.5  
 m)

Hz), 3.82 (3H, s), 3.81 (3H, s), 2.94 (2H, t, J=7.5 Hz), 2.47-2.49 (3H, m), 2.18 (3H, s)

#### Production Example 61

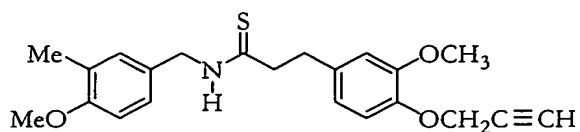
In the same manner way as in the Production Example 40,  
 5 449 mg of  
 N-(4-cyanobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}prop  
 anthioamide (referred as the compound of the present invention  
 61 hereinafter) was obtained from 532 mg of  
 N-(4-cyanobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}prop  
 10 anamide and 435 mg of Lawesson's Reagent.  
 the compound of the present invention 61



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.55 (2H, d, J=7.9 Hz), 7.33 (1H,  
 br.s), 7.12 (2H, d, J=7.9 Hz), 6.93 (1H, d, J=7.9 Hz), 6.72-6.76  
 15 (2H, m), 4.83 (2H, d, J=5.5 Hz), 4.74 (2H, d, J=2.4 Hz), 3.80  
 (3H, s), 3.10 (2H, t, J=7.0 Hz), 2.98 (2H, t, J=7.0 Hz), 2.50  
 (1H, t, J=2.4 Hz)

#### Production Example 62

In the same way as in the Production Example 40, 383 mg  
 20 of  
 N-(4-methoxy-3-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)  
 phenyl}propanthioamide (referred as the compound of the present  
 invention 62 hereinafter) was obtained from 0.55 g of  
 N-(4-methoxy-3-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)  
 25 phenyl}propanamide and 0.44 g of Lawesson's Reagent.  
 the compound of the present invention 62

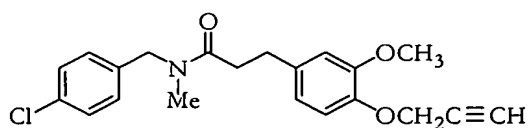


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.89 (1H, br.s), 6.91-6.96 (3H, m),  
 6.68-6.78 (3H, m), 4.72 (2H, d,  $J=2.4$  Hz), 4.59 (2H, d,  $J=4.6$   
 Hz), 3.82 (3H, s), 3.81 (3H, s), 3.08 (2H, t,  $J=7.3$  Hz), 2.91  
 5 (2H, t,  $J=7.3$  Hz), 2.47 (1H, t,  $J=2.4$  Hz), 2.18 (3H, s)

#### Production Example 63

The mixed solution of 500 mg of  
 N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pro  
 panamide and 5 ml of N,N-dimethylformamide was stirred at 0 to  
 10 5 °C, added 61 mg of sodium hydride, and stirred for 30 minutes.  
 Then, 199 mg of methyl iodide was added to the solution, and  
 stirred at 0 to 5 °C for 30 minutes and at room temperature for  
 2 hours. After that, water was added to the reaction mixture  
 and extracted with ethyl acetate. The organic layer was washed  
 15 successively with 5 % hydrochloric acid, saturated aqueous  
 solution of sodium bicarbonate and saturated aqueous solution  
 of sodium chloride, dried by magnesium sulfate, and concentrated  
 under reduced pressure. The residue was purified by silica gel  
 column to obtain 312 mg of  
 20 N-(4-chlorobenzyl)-N-methyl-3-{3-methoxy-4-(2-propynyloxy)p  
 henyl}propanamide (referred as the compound of the present  
 invention 63 hereinafter).

the compound of the present invention 63



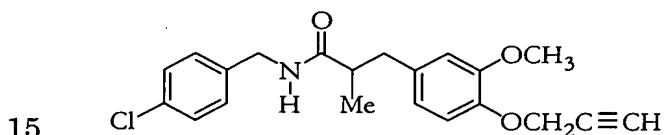
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.26-7.32 (2.2H, m), 7.10-7.15 (1.3H, m), 6.90-7.01 (1.5H, m), 6.66-6.82 (2H, m), 4.70-4.75 (2H, m), 4.54 (2H, s), 4.41 (1H, s), 3.85 (2H, s), 3.82 (1H, s), 2.94-3.01 (2H, m), 2.93 (1H, s), 2.85 (2H, s), 2.59-2.69 (2H, m), 2.47-2.50 (1H, m)

#### Production Example 64

In the same way as in the Production Example 37, 720 mg of

N-(4-chlorobenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 64 hereinafter) was obtained from 934 mg of 2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 496 mg of 4-chlorobenzylamine.

the compound of the present invention 64



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.21-7.26 (2H, m), 6.90-6.96 (3H, m), 6.66-6.71 (2H, m), 5.45 (1H, br.s), 4.74 (2H, d, J=2.4 Hz), 4.38 (1H, dd, J=15 Hz, 6.3 Hz), 4.21 (1H, dd, J=15 Hz, 5.5 Hz), 3.80 (3H, s), 2.87-2.94 (1H, m), 2.64-2.70 (1H, m), 2.49 (1H, t, J=2.4 Hz), 2.42-2.46 (1H, m), 1.23 (3H, d, J=6.8 Hz)

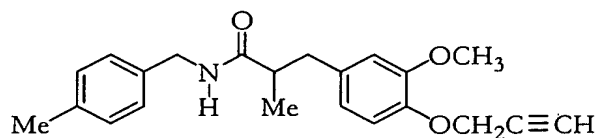
#### Production Example 65

In the same way as in the of Production Example 37, 720 mg of

N-(4-methylbenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 65 hereinafter) was obtained from 934 mg of

2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 424 mg of 4-methylbenzylamine.

the compound of the present invention 65



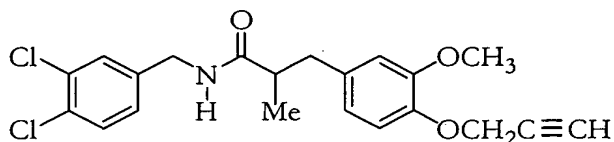
5  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.07 (2H, d,  $J=7.7$  Hz), 6.94 (2H, d,  $J=7.9$  Hz), 6.91 (1H, d,  $J=7.9$  Hz), 6.66-6.71 (2H, m), 5.40 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.20-4.38 (2H, m), 3.80 (3H, s), 2.88-2.97 (1H, m), 2.60-2.68 (1H, m), 2.48 (1H, t,  $J=2.4$  Hz), 2.36-2.45 (1H, m), 2.31 (3H, s), 1.21 (3H, d,  $J=7.0$  Hz)

#### 10 Production Example 66

In the same way as in the Production Example 37, 1.05 g of

N-(3,4-dichlorobenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 66 hereinafter) was obtained from 1.07 g of 2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 704 mg of 3,4-dichlorobenzylamine.

the compound of the present invention 66



20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.32 (1H, d,  $J=8.2$  Hz), 7.21 (1H, d,  $J=1.9$  Hz), 6.91 (1H, d,  $J=7.7$  Hz), 6.81 (1H, dd,  $J=8.2$  Hz, 2.1 Hz), 6.65-6.72 (2H, m), 5.49 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.17-4.38 (2H, m), 3.81 (3H, s), 2.86-2.95 (1H, m), 2.62-2.70 (1H, m), 2.40-2.50 (2H, m), 1.23 (3H, d,  $J=6.7$  Hz)

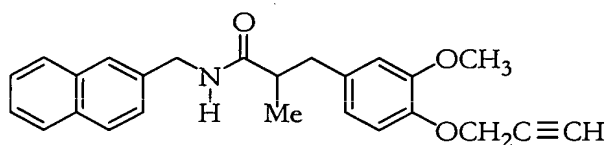


## Production Example 67

In the same way as in the Production Example 37, 480 mg of

N-((naphthalene-2-yl)methyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 67 hereinafter) was obtained from 1.07 g of 2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 628 mg of (naphthalene-2-yl)methylamine.

the compound of the present invention 67



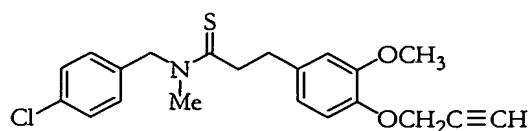
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.71-7.83 (3H, m), 7.53 (1H, s), 7.41-7.50 (2H, m), 7.15 (1H, dd,  $J=8.4$  Hz, 1.7 Hz), 6.86 (1H, d,  $J=7.9$  Hz), 6.72 (1H, d,  $J=1.7$  Hz), 6.69 (1H, dd,  $J=7.9$  Hz, 1.9 Hz), 5.52 (1H, br.s), 4.68 (2H, d,  $J=2.4$  Hz), 4.40-4.60 (2H, m), 3.78 (3H, s), 2.91-2.99 (1H, m), 2.64-2.71 (1H, m), 2.41-2.53 (1H, m), 2.45 (1H, t, 2.4 Hz), 1.25 (3H, d,  $J=6.7$  Hz)

## Production Example 68

In the same way as in the Production Example 40, 242 mg of

N-(4-chloro-benzyl)-N-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 68 hereinafter) was obtained from 500 mg of N-(4-chlorobenzyl)-N-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 390 mg of Lawesson's Reagent.

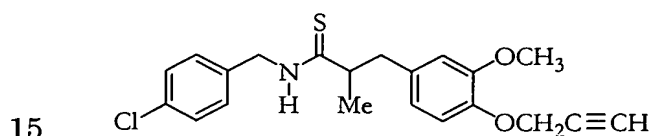
the compound of the present invention 68



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.27 (2H, m), 7.18-7.24 (1.3H, m),  
6.90-7.00 (1.7H, m), 6.66-6.83 (2H, m), 5.29 (1.3H, s), 4.73-4.74  
(2H, m), 4.61 (0.7H, s), 3.85 (2H, s), 3.82 (1H, s), 3.42 (1H,  
5 s), 3.07-3.12 (4H, m), 3.04 (2H, s), 2.48-2.50 (1H, m)

#### Production Example 69

In the same way as in the Production Example 40, 451 mg  
of  
N-(4-chlorobenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)p  
10 henyl}propanthioamide (referred as the compound of the present  
invention 69 hereinafter) was obtained from 420 mg of  
N-(4-chlorobenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)p  
henyl}propanamide and 328 mg of Lawesson's Reagent.  
the compound of the present invention 69



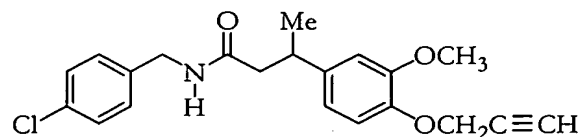
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.23-7.26 (2H, m), 6.96 (1H, br.s),  
6.87-6.93 (3H, m), 6.74 (1H, d, J=1.7 Hz), 6.69 (1H, dd, J=8.1  
Hz, 1.7 Hz), 4.72-4.78 (3H, m), 4.54 (1H, dd, J=15 Hz, 4.8 Hz),  
3.79 (3H, s), 2.97-3.04 (1H, m), 2.75-2.84 (2H, m), 2.49 (1H,  
20 t, J=2.4 Hz), 1.35 (3H, d, J=6.3 Hz)

#### Production Example 70

In the same way as in the Production Example 37, 1.17 g  
of  
N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}but

aneamide (referred as the compound of the present invention 70 hereinafter) was obtained from 934 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyryl chloride and 496 mg of 4-chlorobenzylamine.

5 the compound of the present invention 70



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.20-7.26 (2H, m), 6.93-6.97 (3H, m), 6.72-6.77 (2H, m), 5.50 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.36 (1H, dd,  $J=15$  Hz, 6.0 Hz), 4.22 (1H, dd,  $J=15$  Hz, 5.5 Hz), 3.82 (3H, s), 3.20-3.30 (1H, m), 2.42-2.50 (3H, m), 1.31 (3H, d,  $J=7.0$  Hz)

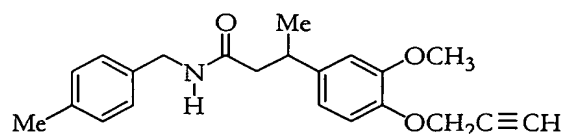
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#### Production Example 71

In the same way as in the Production Example 37, 1.13 g of

15 N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}butaneamide (referred as the compound of the present invention 71 hereinafter) was obtained from 934 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyryl chloride and 424 mg of 4-methylbenzylamine.

20 the compound of the present invention 71



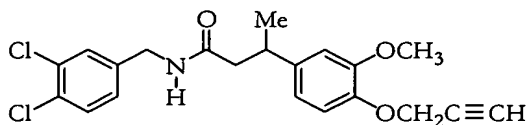
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.08 (2H, d,  $J=7.9$  Hz), 6.92-6.98 (3H, m), 6.73-6.77 (2H, m), 5.43 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.21-4.37 (2H, m), 3.82 (3H, s), 3.22-3.34 (1H, m), 2.48

(1H, t, J=2.4 Hz), 2.38-2.44 (2H, m), 2.31 (3H, s), 1.30 (3H, d, J=7.0 Hz)

#### Production Example 72

5 In the same way as in the Production Example 37, 1.28 g of  
N-(3,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}  
butaneamide (referred as the compound of the present invention  
72 hereinafter) was obtained from 934 mg of  
3-{3-methoxy-4-(2-propynyloxy)phenyl}butyryl chloride and 616  
10 mg of 3,4-dichlorobenzylamine.

the compound of the present invention 72

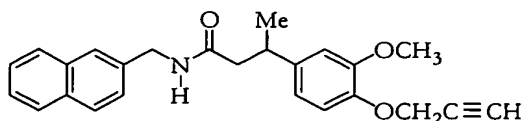


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.32 (1H, d, J=8.3 Hz), 7.21 (1H, d, J=1.7 Hz), 6.96 (1H, d, J=8.5 Hz), 6.81 (1H, dd, J=8.3 Hz, 1.6 Hz), 6.72-6.78 (2H, m), 5.53 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.18-4.34 (2H, m), 3.83 (3H, s), 3.20-3.33 (1H, m), 2.40-2.52 (3H, m), 1.31 (3H, d, J=7.1 Hz)

#### Production Example 73

20 In the same way as in the Production Example 37, 1.21 g of  
N-((naphthalene-2-yl)-methyl)-3-{3-methoxy-4-(2-propynyloxy)  
phenyl}butaneamide (referred as the compound of the present  
invention 73 hereinafter) was obtained from 934 mg of  
3-{3-methoxy-4-(2-propynyloxy)phenyl}butyryl chloride and 550  
25 mg of (naphthalene-2-yl)methylamine.

the compound of the present invention 73



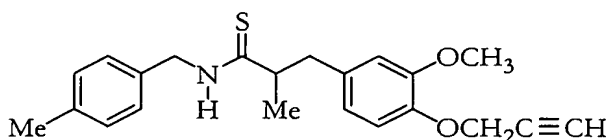
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.72-7.84 (3H, m), 7.54 (1H, s),  
 7.42-7.50 (2H, m), 7.15 (1H, dd, J=8.5 Hz, 1.7 Hz), 6.91 (1H,  
 d, J=8.1 Hz), 6.70-6.78 (2H, m), 5.56 (1H, br.s), 4.68 (2H, m),  
 5 4.42-4.59 (2H, m), 3.80 (3H, s), 3.25-3.36 (1H, m), 2.42-2.49  
 (3H, m), 1.32 (3H, d, J=6.8 Hz)

#### Production Example 74

In the same way as in the Production Example 40, 423 mg  
 of

10 N-(4-methylbenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)p  
 henyl}propanthioamide (referred as the compound of the present  
 invention 74 hereinafter) was obtained from 420 mg of  
 N-(4-methylbenzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)p  
 henyl}propanamide and 348 mg of Lawesson's Reagent.

15 the compound of the present invention 74



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.09 (2H, d, J=7.7 Hz), 6.87-6.95  
 (4H, m), 6.75 (1H, d, J=1.9 Hz), 6.70 (1H, dd, J=8.1 Hz, 1.9  
 Hz), 4.73 (2H, d, J=2.4 Hz), 4.53-4.69 (2H, m), 3.81 (3H, s),  
 20 2.97-3.06 (1H, m), 2.71-2.83 (2H, m), 2.48 (1H, t, J=2.4 Hz),  
 2.32 (3H, s), 1.34 (3H, d, J=6.5 Hz)

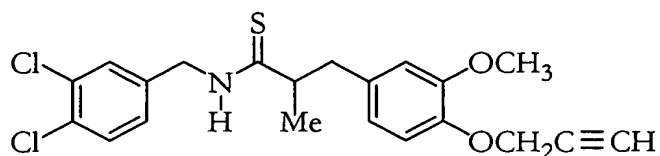
#### Production Example 75

In the same way as in the Production Example 40, 451 mg  
 of

25 N-(3,4-dichloro-benzyl)-2-methyl-3-{3-methoxy-4-(2-propynyl

oxy)phenyl}propanthioamide (referred as the compound of the present invention 75 hereinafter) was obtained from 500 mg of N-(3,4-dichloro-benzyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 357 mg of Lawesson's Reagent.

5 the compound of the present invention 75



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.34 (1H, d, J=8.1 Hz), 7.20 (1H, d, J=1.9 Hz), 6.99 (1H, br.s), 6.91 (1H, d, J=8.0 Hz), 6.68-6.76 (3H, m), 4.74 (2H, d, J=2.4 Hz), 4.55-4.77 (2H, m), 3.81 (3H, s), 2.96-3.05 (1H, m), 2.75-2.85 (2H, m), 2.48 (1H, t, J=2.4 Hz), 1.35 (3H, d, J=6.1 Hz)

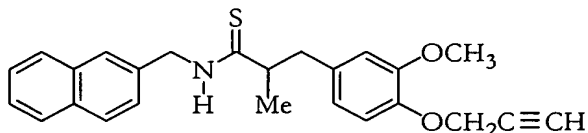
10

#### Production Example 76

In the same way as in the Production Example 40, 1.17 g of

15 N-((naphthalene-2-yl)methyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 76 hereinafter) was obtained from 470 mg of

20 N-((naphthalene-2-yl)methyl)-2-methyl-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 352 mg of Lawesson's Reagent.  
the compound of the present invention 76



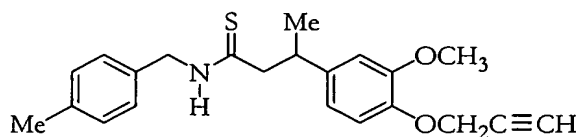
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.74-7.83 (3H, m), 7.45-7.54 (3H, m), 7.07 (1H, dd, J=8.4 Hz, 1.9 Hz), 6.89 (1H, br.s), 6.88 (1H, m),

d, J=7.9 Hz), 6.77 (1H, d, J=1.9 Hz), 6.71 (1H, dd, J=8.2 Hz, 1.9 Hz), 4.73-4.92 (2H, m), 4.69 (2H, d, J=2.4 Hz), 3.80 (3H, s), 2.99-3.09 (1H, m), 2.74-2.85 (2H, m), 2.44 (1H, t, J=2.4 Hz), 1.37 (3H, d, J=6.3 Hz)

# 5 Production Example 77

In the same way as in the Production Example 40, 395 mg of

N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}butanethioamide (referred as the compound of the present invention 10 77 hereinafter) was obtained from 500 mg of N-(4-methylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}butylamide and 412 mg of Lawesson's Reagent. the compound of the present invention 77



15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.09 (2H, d, J=7.7 Hz), 6.93 (1H, d, J=7.9 Hz), 6.89 (2H, d, J=7.9 Hz), 6.84 (1H, br.s), 6.72-6.77 (2H, m), 4.72 (2H, d, J=2.4 Hz), 4.50-4.63 (2H, m), 3.82 (3H, s), 3.36-3.47 (1H, m), 2.93-3.01 (1H, m), 2.72-2.81 (1H, m), 2.48 (1H, t, J=2.4 Hz), 2.32 (3H, s), 1.32 (3H, d, J=7.0 Hz)

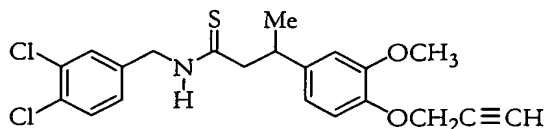
# 20 Production Example 78

In the same way as in the Production Example 40, 313 mg of

N-(3,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}butanethioamide (referred as the compound of the present 25 invention 78 hereinafter) was obtained from 500 mg of N-(3,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl

}butaneamide and 343 mg of Lawesson's Reagent.

the compound of the present invention 78



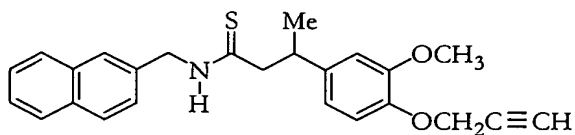
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.34 (1H, d, J=8.3 Hz), 7.20 (1H,  
5 d, J=1.9 Hz), 7.01 (1H, br.s), 6.91-6.96 (1H, m), 6.70-6.77 (3H,  
m), 4.73 (2H, d, J=2.4 Hz), 4.51-4.72 (2H, m), 3.82 (3H, s),  
3.34-3.47 (1H, m), 2.97-3.05 (1H, m), 2.76-2.83 (1H, m), 2.49  
(1H, t, J=2.4 Hz), 1.33 (3H, d, J=7.1 Hz)

Production Example 79

10 In the same way as in the Production Example 40, 436 mg  
of

N-((naphthalene-2-yl)methyl)-3-(3-methoxy-4-(2-propynyloxy)  
phenyl}butanethioamide (referred as the compound of the present  
invention 79 hereinafter) was obtained from 500 mg of  
15 N-((naphthalene-2-yl)methyl)-3-(3-methoxy-4-(2-propynyloxy)  
phenyl}butaneamide and 388 mg of Lawesson's Reagent.

the compound of the present invention 79



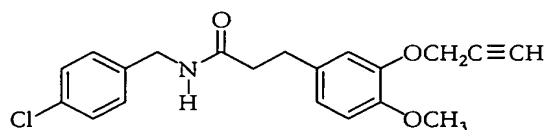
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.75-7.81 (3H, m), 7.46-7.52 (3H,  
20 m), 7.06 (1H, dd, J=8.3 Hz, 1.8 Hz), 6.93 (1H, br.s), 6.87 (1H,  
d, J=7.9 Hz), 6.77 (1H, d, J=1.9 Hz), 6.74 (1H, dd, J=8.1 Hz,  
1.9 Hz), 4.71-4.85 (2H, m), 4.64 (2H, d, J=2.4 Hz), 3.79 (3H,  
s), 3.36-3.49 (1H, m), 2.98-3.06 (1H, m), 2.76-2.84 (1H, m),  
2.43 (1H, t, J=2.4 Hz), 1.34 (3H, d, J=7.0 Hz)



## Production Example 80

566 mg of 4-chlorobenzylamine, 937 mg of 3-{4-methoxy-3-(2-propynyloxy)phenyl}propionic acid, 805 mg of 1-ethyl-3-(3-diethylaminopropyl)carbodiimide hydrochloride (referred as WSC hereinafter) and 10 ml of N,N-dimethylformamide were mixed at room temperature for 4 hours. Then water was added to the residue and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 847 mg of N-(4-chlorobenzyl)-3-{4-methoxy-3-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 80 hereinafter).

the compound of the present invention 80



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.22-7.27 (2H, m), 7.05 (2H, d, J=7.5 Hz), 6.76-6.89 (3H, m), 5.55 (1H, br.s), 4.72 (2H, d, J=2.4 Hz), 4.34 (2H, d, J=5.7 Hz), 3.84 (3H, s), 2.93 (2H, t, J=7.4 Hz), 2.44-2.53 (3H, m)

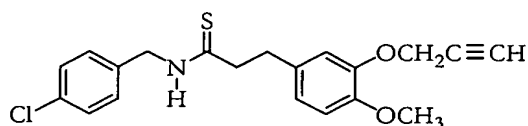
## Production Example 81

517 mg of N-(4-chlorobenzyl)-3-{4-methoxy-3-(2-propynyloxy)phenyl}propanamide, 419 mg of Lawesson's Reagent and 10 ml of tetrahydrofuran were mixed, and stirred at 65 °C for 5 hours. Then the reaction

mixture was cooled, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 160 mg of

5 N-(4-chlorobenzyl)-3-{4-methoxy-3-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 81 hereinafter).

the compound of the present invention 81



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.24-7.26 (3H, m), 7.01 (2H, d, -  
10 J=8.2 Hz), 6.88 (1H, d, J=1.4 Hz), 6.73-6.77 (2H, m), 4.72 (2H, d, J=2.4 Hz), 4.67 (2H, d, J=5.3 Hz), 3.84 (3H, s), 3.07 (2H, t, J=7.0 Hz), 2.95 (2H, t, J=7.0 Hz), 2.44 (1H, t, J=2.4 Hz)  
Production Example 82

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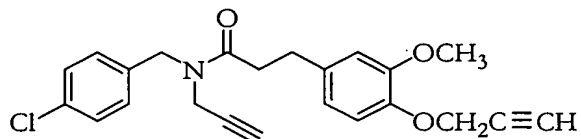
mg

of

15 N-(4-chlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 5 ml of N,N-dimethylformamide were mixed and cooled to 0 °C. 72 mg of sodium hydride was added to the mixture, and it was stirred at 0 °C for about 15 minutes. Then, 196 mg of propargyl bromide was added in it, the mixture was stirred at  
20 0 °C for 30 minutes and at room temperature for 2 hours. After that, water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride,  
25 dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain

105 mg of  
N-(4-chlorobenzyl)-N-propynyl-3-{4-methoxy-3-(2-propynyloxy)  
)phenyl}propanamide (referred as the compound of the present  
invention 82 hereinafter).

5 the compound of the present invention 82

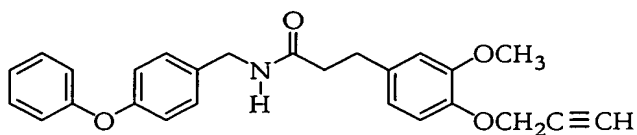


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.26-7.30 (2H, m), 7.16 (1H, d, -  
J=8.2 Hz), 7.02 (1H, d, J=8.2 Hz), 6.91-6.97 (1H, m), 6.67-6.82  
(2H, m), 4.73 (2H, d, J=2.1 Hz), 4.64 (1H, s), 4.54 (1H, s),  
10 4.20 (1H, s), 3.84 (3H, s), 3.82 (1H, s), 2.90-3.03 (2H, m),  
2.75 (1H, t, J=7.6 Hz), 2.62 (1H, t, J=7.5 Hz), 2.49 (1H, t,  
J=2.1 Hz), 2.26 (0.5H, s), 2.19 (0.5H, s)

#### Production Example 83

943 mg of 4-phenoxybenzylamine hydrochloride, 1.01 g of  
15 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 844 mg of  
WSC and 10 ml of pyridine were mixed at room temperature for  
4 hours. Then water was added to the reaction mixture and extracted  
with ethyl acetate. The organic layer was washed successively  
with 5 % hydrochloric acid, water and saturated aqueous solution  
20 of sodium chloride, dried by magnesium sulfate, and concentrated  
under reduced pressure. The residue was purified by silica gel  
column to obtain 1.31 g of  
N-(4-phenoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}pr  
opamide (referred as the compound of the present invention  
25 83 hereinafter).

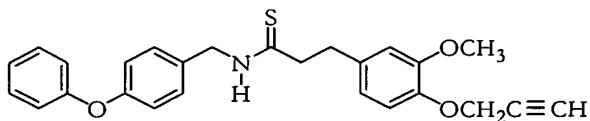
the compound of the present invention 83



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.30-7.36 (2H, m), 7.08-7.15 (3H, m), 6.92-7.01 (5H, m), 6.75 (1H, d,  $J=1.9$  Hz), 6.73 (1H, dd,  $J=8.2$  Hz, 2.2 Hz), 5.61 (1H, br.s), 4.71 (2H, d,  $J=2.4$  Hz), 4.38 (2H, d,  $J=5.5$  Hz), 3.83 (3H, s), 2.95 (2H, t,  $J=7.5$  Hz), 2.50 (2H, t,  $J=7.5$  Hz), 2.46 (1H, t,  $J=2.4$  Hz)

#### Production Example 84

In the same way as in the Production Example 40, 250 mg of  
 10 N-(4-phenoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 84 hereinafter) was obtained from 1.0 g of N-(4-phenoxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propameamide and 681 mg of Lawesson's Reagent.  
 15 the compound of the present invention 84



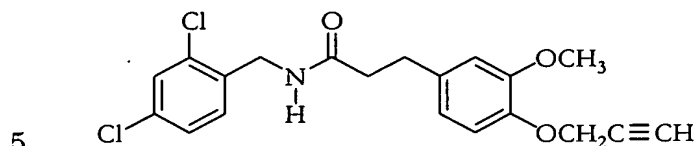
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.31-7.37 (2H, m), 7.03-7.15 (4H, m), 6.90-7.02 (5H, m), 6.70-6.78 (2H, m), 4.60-4.70 (4H, m), 3.82 (3H, s), 3.09 (2H, t,  $J=7.2$  Hz), 2.93 (2H, t,  $J=7.2$  Hz),  
 20 2.44 (1H, t,  $J=2.4$  Hz)

#### Production Example 85

By using 300 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 209 mg of 2,4-dichlorobenzylamine according to the Production  
 25 Example 5 was obtained 450 mg of

N-(2,4-dichlorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 85 hereinafter).

the compound of the present invention 85



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.34 (1H, d,  $J=1.9$  Hz), 7.11-7.19 (2H, m), 6.92 (1H, d,  $J=8.0$  Hz), 6.68-6.71 (2H, m), 5.78 (1H, br.s), 4.73 (2H, d,  $J=2.5$  Hz), 4.43 (2H, d,  $J=6.1$  Hz), 3.81 (3H, s), 2.92 (2H, t,  $J=7.5$  Hz), 2.48-2.52 (3H, m)

10 Production Example 86

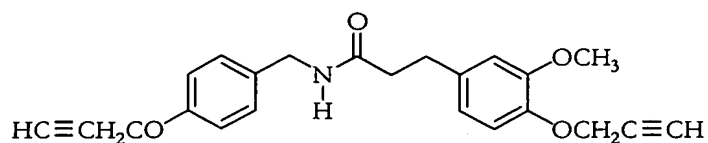
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g

of

N-(4-hydroxybenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 418 mg of propargyl bromide, 531 mg of potassium carbonate and 15 ml of acetonitrile were mixed, and stirred at 80 °C for 3 hours. Then the reaction mixture was cooled to room temperature, and water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 1.12 g of N-{4-(2-propynyloxy)benzyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 86 hereinafter).

25 the compound of the present invention 86



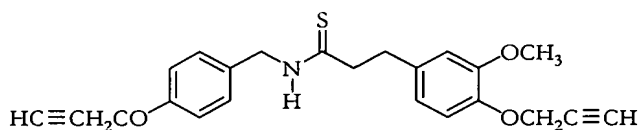
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.09 (2H, d,  $J=8.5$  Hz), 6.88-6.95 (3H, m), 6.70-6.75 (2H, m), 5.61 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.68 (2H, d,  $J=2.4$  Hz), 4.33 (2H, d,  $J=5.6$  Hz), 3.81 (3H, s), 2.93 (2H, t,  $J=7.4$  Hz), 2.46-2.53 (4H, m)

#### Production Example 87

In the same way as in the Production Example 40, 780 mg of

N-{4-(2-propynyloxy)benzyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 87 hereinafter) was obtained from 793 mg of N-{4-(2-propynyloxy)benzyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 594 mg of Lawesson's Reagent.

the compound of the present invention 87



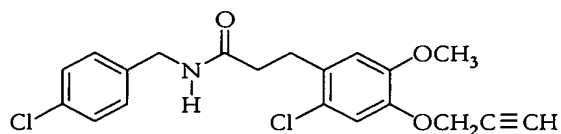
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.04-7.09 (2H, m), 7.03 (1H, br.s), 6.90-6.94 (3H, m), 6.75 (1H, d,  $J=1.9$  Hz), 6.72 (1H, dd,  $J=8.0$  Hz, 1.9 Hz), 4.73 (2H, d,  $J=2.4$  Hz), 4.69 (2H, d,  $J=2.4$  Hz), 4.64 (2H, d,  $J=5.1$  Hz), 3.81 (3H, s), 3.08 (2H, t,  $J=7.1$  Hz), 2.92 (2H, t,  $J=7.2$ ), 2.52 (1H, t,  $J=2.4$  Hz), 2.49 (1H, t,  $J=2.4$ )

#### Production Example 88

1.9 g of N-(4-chlorobenzyl)-3-{2-chloro-5-methoxy-4-hydroxyphenyl}propanamide, 0.57 ml of propargyl bromide, 1.0 g of potassium

carbonate and 40 ml of acetonitrile were mixed, and stirred at 80 °C for 1 hour. Then the reaction mixture was cooled to room temperature, and ethyl acetate was added to the reaction mixture and filtered. The filtrate was concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 1.9 g of N-(4-cholorobenzyl)-3-{2-chloro-5-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 88 hereinafter).

the compound of the present invention 88

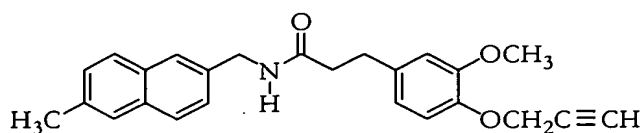


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.26 (2H, d, J=8.3 Hz), 7.04 (2H, d, J=8.3 Hz), 7.04 (1H, s), 6.78 (1H, s), 5.71 (1H, br.s), 4.73 (2H, d, J=2.2 Hz), 4.36 (2H, d, J=5.9 Hz), 3.79 (3H, s), 3.04 (2H, t, J=7.4 Hz), 2.50-2.54 (3H, m)

Production Example 89

By using 586 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 519 mg of (6-methylnaphthalene-2-yl)methylamine hydrochloride according to the Production Example 83 was obtained 850 mg of N-(6-methylnaphthalene-2-yl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 89 hereinafter).

the compound of the present invention 89

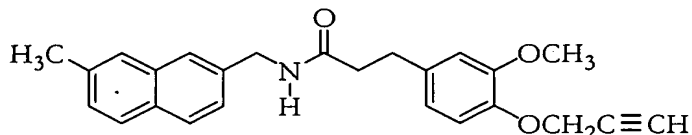


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.68 (2H, t, J=9.1 Hz), 7.57 (2H, d, J=5.1 Hz), 7.31 (1H, d, J=8.3 Hz), 7.23 (1H, d, J=8.3 Hz), 6.91 (1H, d, J=8.3 Hz), 6.70-6.77 (2H, m), 5.63 (1H, br.s), 4.70 (2H, d, J=2.4 Hz), 4.55 (2H, d, J=5.5 Hz), 3.80 (3H, s), 2.97 (2H, t, J=7.5 Hz), 2.49-2.56 (5H, m), 2.46 (1H, t, J=2.4 Hz)

#### Production Example 90

By using 810 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 720 mg of (7-methylnaphthalene-2-yl)methylamine hydrochloride according to the Production Example 83 was obtained 730 mg of N-(7-methylnaphthalene-2-yl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 90 hereinafter).

the compound of the present invention 90



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.68-7.75 (2H, m), 7.53 (1H, s), 7.52 (1H, s), 7.29 (1H, dd, J=8.4 Hz, 1.7 Hz), 7.19 (1H, dd, J=8.2 Hz, 1.7 Hz), 6.91 (1H, d, J=8.2 Hz), 6.76 (1H, d, J=1.9 Hz), 6.73 (1H, dd, J=8.0 Hz, 1.9 Hz), 5.64 (1H, br.s), 4.70 (2H, d, J=2.4 Hz), 4.54 (2H, d, J=5.5 Hz), 3.80 (3H, s), 2.96 (2H, t, J=7.5 Hz), 2.49-4.56 (5H, m), 2.46 (1H, t, J=2.4 Hz)

#### Production Example 91

In the same way as in the Production Example 40, 292 mg

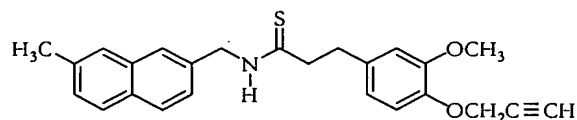


of

N-(7-methylnaphthalene-2-yl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanthioamide (referred as the compound of the present invention 91 hereinafter) was obtained from 420 mg of

5 N-(7-methylnaphthalene-2-yl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 310 mg of Lawesson's Reagent.

the compound of the present invention 91



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.74 (1H, d, J=8.2 Hz), 7.72 (1H, d, J=8.4 Hz), 7.55 (1H, s), 7.51 (1H, s), 7.32 (1H, dd, J=8.3 Hz, 1.5 Hz), 7.13 (1H, dd, J=8.2 Hz, 1.7 Hz), 7.10 (1H, br.s), 6.88 (1H, d, J=8.2 Hz), 6.77 (1H, d, J=1.9 Hz), 6.72 (1H, dd, J=8.3 Hz, 1.8 Hz), 4.85 (2H, d, J=5.1 Hz), 4.67 (2H, d, J=2.4 Hz), 3.80 (3H, s), 2.96 (2H, t, J=7.2 Hz), 3.10 (2H, t, J=7.2 Hz), 2.51 (3H, s), 2.44 (1H, t, J=2.4 Hz)

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Production Example 92

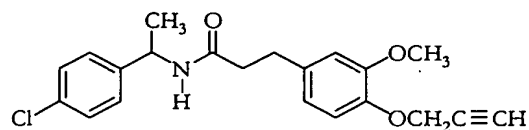
0.2 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.12 g of 1-(4-chlorophenyl)ethylamine, 0.2 ml of triethylamine and 5 ml of tetrahydrofuran were mixed, and stirred

20 at room temperature for 30 minutes. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % of hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate,

25 and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.21 g of N-{1-(4-chlorophenyl)ethyl}-3-{3-methoxy-4-(2-propynyloxy)p

henyl}propanamide (referred as the compound of the present invention 92 hereinafter).

the compound of the present invention 92



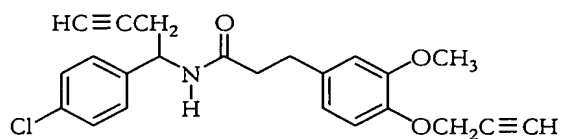
5  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.25-7.27 (2H, m), 7.09 (2H, d,  $J=8.0$  Hz), 6.93 (1H, d,  $J=8.0$  Hz), 6.69-6.71 (2H, m), 5.67 (1H, br.d), 5.03-5.06 (1H, m), 4.73-4.74 (2H, m), 3.80 (3H, s), 2.91 (2H, t,  $J=6.8$  Hz), 2.41-2.47 (3H, m), 1.38 (3H, d,  $J=7.0$  Hz)

Production Example 93

10 By using 0.84 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 0.85 g of 1-(4-chlorophenyl)-3-butynylamine according to the Production Example 92 was obtained 0.40 g of

15 N-{1-(4-chlorophenyl)-3-butynyl}-3-{3-methoxy-4-(2-propynyl oxy)phenyl}propanamide (referred as the compound of the present invention 93 hereinafter).

the present invention 93

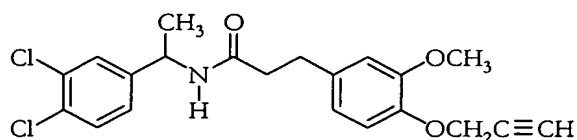


20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.28 (2H, d,  $J=8.5$  Hz), 7.12 (2H, d,  $J=8.5$  Hz), 6.95 (1H, d,  $J=8.8$  Hz), 6.72-6.74 (2H, m), 5.85 (1H, br.d,  $J=8.1$  Hz), 5.14 (1H, dt,  $J=8.0$  Hz, 5.6 Hz), 4.75 (2H, d,  $J=2.2$  Hz), 3.80 (3H, s), 2.93 (2H, t,  $J=7.1$  Hz), 2.63-2.67 (2H, m), 2.47-2.57 (3H, m), 1.99 (1H, t,  $J=2.7$  Hz)

Production Example 94

0.30 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 0.24 g of 1-(3,4-dichlorophenyl)ethylamine, 0.26 g of WSC and 10 ml of dimethylformamide were mixed, and stirred at room temperature for 3 hours. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.25 g of N-{1-(3,4-dichlorophenyl)ethyl}-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 94 hereinafter).

the compound of the present invention 94



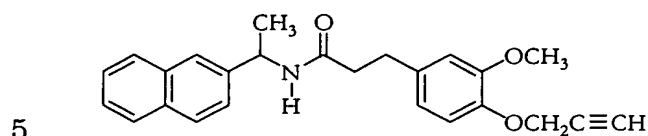
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.34 (1H, d,  $J=8.5$  Hz), 7.30 (1H, d,  $J=2.2$  Hz), 6.98 (1H, dd,  $J=8.5$  Hz, 2.2 Hz), 6.94 (1H, d,  $J=8.2$  Hz), 6.70-6.72 (2H, m), 5.67 (1H, br.d,  $J=7.5$  Hz), 5.00-5.04 (1H, m), 4.74 (2H, d,  $J=2.5$  Hz), 3.81 (3H, s), 2.91 (2H, t,  $J=7.2$  Hz), 2.47-2.50 (3H, m), 1.37 (3H, d,  $J=6.8$  Hz)

#### Production Example 95

By using 0.30 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 0.29 g of 1-(naphthalene-2-yl)ethylamine according to the Production Example 94 was obtained 0.23 g of

N-{1-(naphthalene-2-yl)ethyl}3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 95 hereinafter).

the present invention 95



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.78-7.90 (3H, m), 7.65 (1H, s), 7.47-7.48 (2H, m), 7.28-7.30 (1H, m), 6.90 (1H, d,  $J=8.0$  Hz), 6.70-6.72 (2H, m), 5.60 (1H, br.d,  $J=7.0$  Hz), 5.31-5.24 (1H, m), 4.70 (2H, m), 3.76 (3H, s), 2.93 (2H, t,  $J=7.2$  Hz), 2.46-2.50 (3H, m), 1.51 (3H, d,  $J=6.8$  Hz)

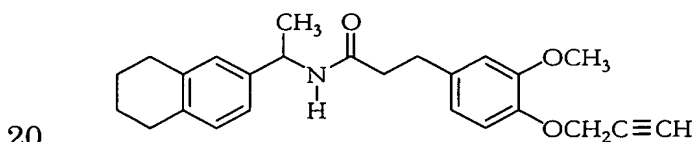
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Production Example 96

By using 0.30 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 0.22 g of 1-(5,6,7,8-tetrahydronaphthalene-2-yl)ethylamine according to the Production Example 94 was obtained 0.22 g of N-{1-(5,6,7,8-tetrahydronaphthalene-2-yl)ethyl}3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 97 hereinafter).

15

the present invention 96



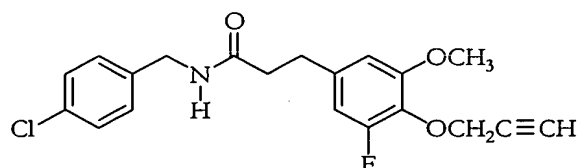
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.01 (1H, d,  $J=8.5$  Hz), 6.92-6.95 (3H, m), 6.71-6.73 (2H, m), 5.47 (1H, br.d,  $J=7.2$  Hz), 5.00-5.07 (1H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.81 (3H, s), 2.92 (2H, t,  $J=7.5$  Hz), 2.70-2.75 (4H, m), 2.48 (1H, t,  $J=2.5$  Hz), 2.44 (2H, t,

$J=7.5$  Hz), 1.76-1.86 (4H, m), 1.40 (3H, d,  $J=7.0$  Hz)

# Production Example 97

By using 0.30 g of 3-{3-fluoro-5-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 0.22 g of 4-chlorobenzylamine according to the Production Example 94 was obtained 0.23 g of N-(4-chlorobenzyl)-3-{3-fluoro-5-methoxy-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 97 hereinafter).

10 the compound of the present invention 97

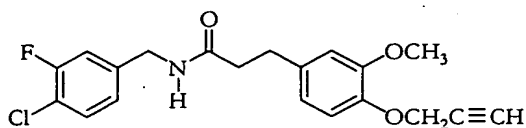


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.28 (2H, d,  $J=8.3$  Hz), 7.11 (2H, d,  $J=8.3$  Hz), 6.54-6.58 (2H, m), 5.65 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.38 (2H, d,  $J=5.9$  Hz), 3.81 (3H, s), 2.93 (2H, t,  $J=7.5$  Hz), 2.49 (2H, t,  $J=7.5$  Hz), 2.45 (1H, t,  $J=2.4$  Hz)

# Production Example 98

By using 196 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 234 mg of 4-chloro-3-fluorobenzylamine hydrochloride according to the Production Example 83 was obtained 310 mg of N-(4-chloro-3-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 98 hereinafter).

the compound of the present invention 98

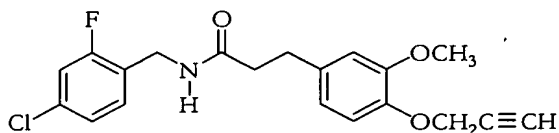


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.30 (1H, t, J=7.8 Hz), 6.92-6.98 (2H, m), 6.82-6.86 (1H, m), 6.71-6.76 (2H, m), 5.66 (1H, br.s), 4.74 (2H, d, J=2.4 Hz), 4.36 (2H, d, J=6.1 Hz), 3.83 (3H, s), 2.95 (2H, t, J=7.4 Hz), 2.52 (2H, t, J=7.4 Hz), 2.49 (1H, t, J=2.4 Hz)

#### Production Example 99

By using 196 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 234 mg of 4-chloro-2-fluorobenzylamine hydrochloride according to the Production Example 83 was obtained 330 mg of N-(4-chloro-2-fluorobenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 99 hereinafter).

the compound of the present invention 99



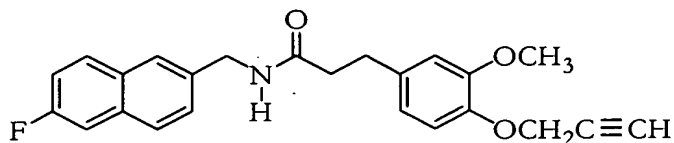
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.03-7.15 (3H, m), 6.92 (1H, d, J=8.0 Hz), 6.67-6.72 (2H, m), 5.69 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.39 (2H, d, J=6.1 Hz), 3.81 (3H, s), 2.92 (2H, t, J=7.5 Hz), 2.46-2.51 (3H, m)

#### Production Example 100

By using 562 mg of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid and 508 mg of (6-fluoronaphthalene-2-yl)methylamine hydrochloride

according to the Production Example 83 was obtained 540 mg of N-((6-fluoronaphthalene-2-yl)methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 100 hereinafter).

5 the compound of the present invention 100



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.70-7.78 (2H, m), 7.59 (1H, s), 7.42 (1H, dd, J=9.8 Hz, 2.2 Hz), 7.22-7.30 (2H, m), 6.91 (1H, d, J=8.0 Hz), 6.72-6.77 (2H, m), 5.68 (1H, br.s), 4.71 (2H, d, J=2.4 Hz), 4.55 (2H, d, J=5.6 Hz), 3.79 (3H, s), 2.97 (2H, t, J=7.1 Hz), 2.53 (2H, t, J=7.1 Hz), 2.46 (1H, t, J=2.4 Hz)

10

Production Example 101

10.7 g of 4-(2-methyl-[1,3]dioxolane-2-yl)benzylamine, 11.8 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 10.6 g of WSC and 150 ml of dimethylformamide were mixed at room temperature for 2 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. About 100 ml of acetone and about 0.1 g of p-toluenesulfonic acid were added to the residue, then the mixture was stirred at 50 °C for 3 hours. The mixture was cooled, added saturated aqueous solution of sodium bicarbonate was added to the mixture, and concentrated. Ethyl acetate was added to the residue, washed with water, dried by dried by magnesium sulfate, and concentrated under reduced

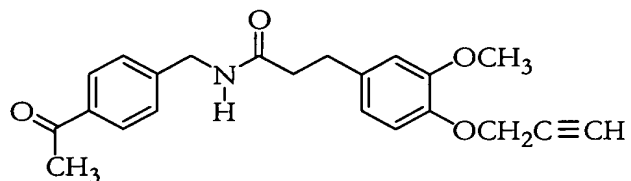
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25

pressure. The obtained solid was washed by hexane to obtain 12.5 g of N-(4-methylcarbonylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 101 hereinafter).

the compound of the present invention 101



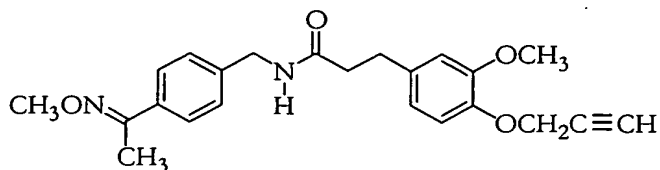
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.87 (2H, d,  $J=8.3$  Hz), 7.20 (2H, d,  $J=8.3$  Hz), 6.94 (1H, d,  $J=7.5$  Hz), 6.72-6.74 (2H, m), 5.73 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.50 (2H, d,  $J=6.3$  Hz), 3.81 (3H, s), 2.59 (3H, s), 2.53 (2H, t,  $J=7.5$  Hz), 2.96 (2H, t,  $J=7.5$  Hz), 2.50 (1H,  $J=2.4$  Hz)

#### Production Example 102

0.52 g of N-(4-methylcarbonylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.18 g of O-methoxyhydroxylamine hydrochloride, 0.16 ml of pyridine and 10 ml of ethanol were mixed, and stirred at 50 °C for 2 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid twice, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.49 g of N-(4-(1-methoxyiminoethyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present



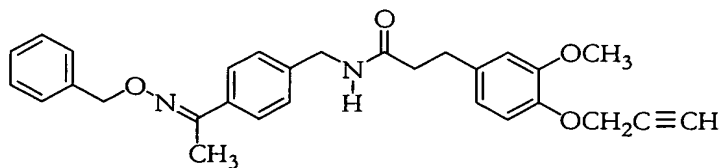
invention 102 hereinafter).



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.58 (2H, d,  $J=8.0$  Hz), 7.40 (2H, d,  $J=8.0$  Hz), 6.94 (1H, d,  $J=8.0$  Hz), 6.71-6.75 (2H, m), 5.59 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.41 (2H, d,  $J=6.0$  Hz), 3.98 (3H, s), 3.82 (3H, s), 2.95 (2H, t,  $J=7.6$  Hz), 2.49-2.52 (3H, m), 2.20 (3H, s)

Production Example 103

0.50 g of  
 10 N-(4-methylcarbonylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.26 g of O-benzyloxyhydroxylamine hydrochloride, 0.12 ml of pyridine and 10 ml of ethanol were mixed, and stirred at 50 °C for 2 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The  
 15 organic layer was washed successively with 5 % hydrochloric acid twice, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.54 g of  
 20 N-(4-(1-benzyloxyiminoethyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 103 hereinafter).



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.57 (2H, d,  $J=7.9$  Hz), 7.20-7.46

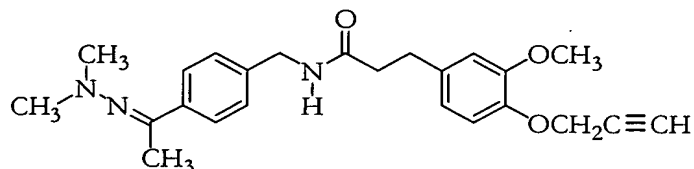
(5H, m), 7.13 (2H, d, J=7.9 Hz), 6.93 (1H, d, J=7.5 Hz), 6.71-6.74 (2H, m), 5.58 (1H, br.s), 5.53 (2H, s), 4.71-4.72 (2H, m), 4.39 (2H, d, J=5.5 Hz), 3.81 (3H, s), 2.94 (2H, t, J=7.5 Hz), 2.48-2.51 (3H, m), 2.24 (3H, s)

# 5 Production Example 104

0.50 g of

N-(4-methylcarbonylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.21 ml of 1,1-dimethylhydrazine, 1 ml of acetic acid and 10 ml of methanol were mixed, and stirred under the condition of reflux for 1 hour. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid twice, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.46 g of N-(4-(1-dimethylaminoimino)ethyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 104 hereinafter).

20 the compound of the present invention 104

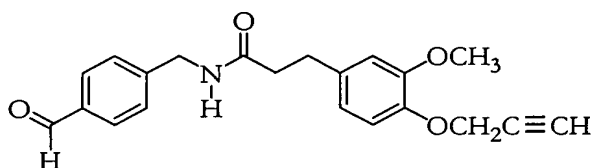


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.66 (2H, d, J=8.0 Hz), 7.14 (2H, d, J=8.0 Hz), 6.94 (1H, d, J=8.0 Hz), 6.72-6.76 (2H, m), 5.58 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.41 (2H, d, J=5.6 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.2 Hz), 2.59 (6H, s), 2.48-2.52 (3H, m), 2.33 (3H, s)

## Production Example 105

By using 13.0 g of 4-([1,3]dioxolane-2-yl)benzylamine and 15.5 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid according to the Production Example 101 was obtained 14.7 g of  
 5 N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 105 hereinafter).

the compound of the present invention 105

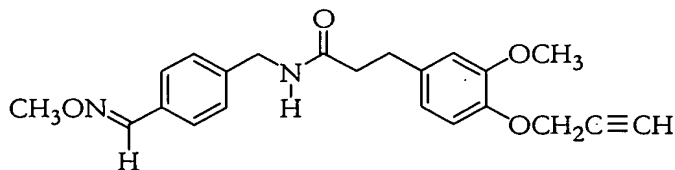


10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 9.98 (1H, s), 7.79-7.81 (2H, m), 7.26-7.28 (2H, m), 6.35 (1H, d,  $J=7.9$  Hz), 6.71-6.75 (2H, m), 5.74 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.48 (2H, d,  $J=5.5$  Hz), 3.82 (3H, s), 2.96 (2H, t,  $J=7.5$  Hz), 2.55 (2H, t,  $J=7.5$  Hz), 2.50 (2H, t,  $J=2.4$  Hz)

## 15 Production Example 106

By using 0.54 g of N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.15 g of O-methoxyhydroxylamine hydrochloride according to the Production Example 102 was obtained 0.54 g of  
 20 N-(4-methoxyiminomethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}-propanamide (referred as the compound of the present invention 106 hereinafter).

the compound of the present invention 106

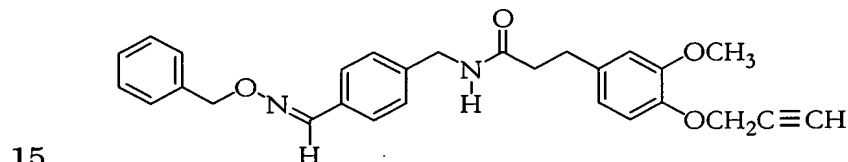


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.03 (1H, s), 7.51 (2H, d, J=8.0 Hz), 7.14 (2H, d, J=8.0 Hz), 6.94 (1H, d, J=8.0 Hz), 6.72-6.76 (2H, m), 5.61 (1H, br.s), 4.74 (2H, d, J=2.4 Hz), 4.42 (2H, d, J=4.8 Hz), 3.97 (3H, s), 3.82 (3H, s), 2.95 (2H, t, J=7.6 Hz),  
 5 2.48-2.53 (3H, m)

#### Production Example 107

By using 0.56 g of N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.31 g of O-benzyloxyhydroxylamine hydrochloride according to the Production Example 103 was obtained 0.64 g of N-(4-benzyloxyiminomethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 107 hereinafter).

the compound of the present invention 107



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.10 (1H, s), 7.50 (2H, d, J=8.1 Hz), 7.29-7.42 (5H, m), 7.13 (2H, d, J=8.1 Hz), 6.93 (1H, d, J=7.9 Hz), 6.71-6.74 (2H, m), 5.58 (1H, br.s), 5.20 (2H, s), 4.72 (2H, d, J=2.4 Hz), 4.40 (2H, d, J=5.5 Hz), 3.82 (3H, s),  
 20 2.95 (2H, t, J=7.5 Hz), 2.48-2.53 (3H, m)

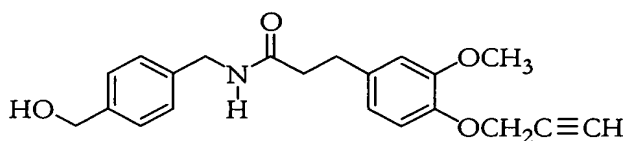
#### Production Example 108

3.48 g of N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 50 ml of ethanol were mixed, and 0.10 g of sodium borohydride was mixed with it at 0 °C and followed by stirring at room temperature for 3 hours, then 0.10 g of sodium borohydride

25

was added again followed by stirring at room temperature for 1 hour. After that, saturated aqueous solution of ammonium chloride and water were added to the reaction mixture, then concentrated under reduced pressure. The residue was extracted with ethyl acetate. The organic layer was washed successively with saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 3.7 g of N-(4-hydroxymethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 108 hereinafter).

the compound of the present invention 108



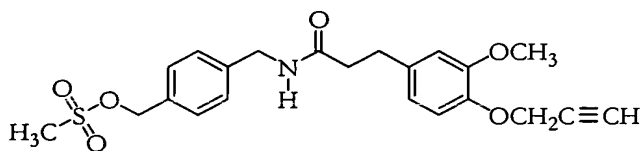
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.29 (2H, d,  $J=7.9$  Hz), 7.13 (2H, d,  $J=7.9$  Hz), 6.93 (1H, d,  $J=8.7$  Hz), 6.70-6.73 (2H, m), 5.58 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.67 (2H, d,  $J=5.5$  Hz), 4.38 (2H, d,  $J=5.9$  Hz), 3.81 (3H, s), 2.94 (2H, t,  $J=7.3$  Hz), 2.48-2.51 (3H, m), 1.75 (1H, br.t)

Production Example 109

1.5 g of N-(4-hydroxymethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide, 0.71 ml of triethylamine and 50 ml of tetrahydrofuran were mixed, 0.35 ml of methansulfonyl chloride was mixed with it at  $0^\circ\text{C}$  and followed by stirring at room temperature for 30 minutes. Then water was added to the residue and concentrated under reduced pressure. The residue was

extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 1.7 g of 4-((3-(3-methoxy-4-(2-propynyloxy)phenyl)propionyl)aminomethyl)benzyl methansulfonate (referred as the compound of the present invention 109 hereinafter).

the compound of the present invention 109



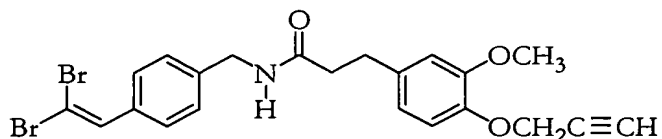
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.34 (2H, d,  $J=8.1$  Hz), 7.16 (2H, d,  $J=8.1$  Hz), 6.95 (1H, d,  $J=7.9$  Hz), 6.72-6.75 (2H, m), 5.61 (1H, br.s), 5.21 (2H, s), 4.74 (2H, d,  $J=2.8$  Hz), 4.42 (2H, d,  $J=5.5$  Hz), 3.82 (3H, s), 2.94-2.97 (5H, m), 3.82 (3H, s), 2.49-2.54 (3H, m)

Production Example 110

1.2 g of N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide and 30 ml of methylene chloride were mixed, 5.3 g of triphenylphosphine and 3.6 g of carbontetrabromide were mixed with it under ice cooling followed by stirring under ice cooling for 2 hours. Then ethyl acetate was added to the reaction mixture, and it was washed successively with saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column

to obtain 0.2 g of N-(4-(2,2-dibromovinyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 110 hereinafter).

5 the compound of the present invention 110



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.75-7.47 (3H, m), 7.13 (2H, d,  $J=7.9$  Hz), 6.94 (1H, d,  $J=7.9$  Hz), 6.72-6.75 (2H, m), 5.60 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.39 (2H, d,  $J=5.9$  Hz), 3.82 (3H, s), 2.95 (2H, t,  $J=7.1$  Hz), 2.48-2.53 (3H, m)

Production Example 111

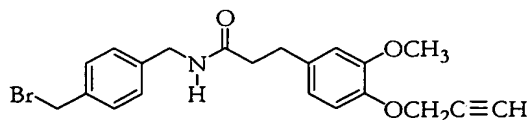
0.37 g of

4-((3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl)aminomethyl)benzyl methansulfonate, 2.0 g of lithium bromide and 20 ml of acetone were mixed, and stirred under the condition of reflux for 3 hours. Then ethyl acetate was added to the reaction mixture.

It was washed with water, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.34 g of

20 N-(4-bromomethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 111 hereinafter).

the compound of the present invention 111



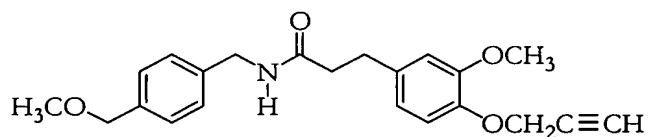
25  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.32 (2H, d,  $J=8.0$  Hz), 7.11 (2H,

d, J=8.0 Hz), 6.95 (1H, d, J=8.2 Hz), 6.71-6.75 (2H, m), 5.59 (1H, br.s), 4.74 (2H, d, J=2.4 Hz), 4.72 (2H, s), 4.67 (2H, d, J=5.1 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.48-2.52 (3H, m)

# 5 Production Example 112

0.23 g of 4-((3-(3-methoxy-4-(2-propynyloxy)phenyl)propionyl)aminomethyl)benzyl methansulfonate, 0.11 g of sodium methoxied (28 % methanol solution) and 5 ml of tetrahydrofuran were mixed and stirred at room temperature for 2 hours. Then ethyl acetate was added to the reaction mixture. It was washed with water and saturated aqueous solution of sodium bicarbonate, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.15 g of N-(4-methoxymethylbenzyl)-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide (referred as the compound of the present invention 112 hereinafter).

the compound of the present invention 112



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.27 (2H, d, J=7.9 Hz), 7.14 (2H, d, J=7.9 Hz), 6.93 (1H, d, J=8.3 Hz), 6.71-6.75 (2H, m), 5.58 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.43 (2H, s), 4.40 (2H, d, J=5.5 Hz), 3.82 (3H, s), 3.37 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.48-2.53 (3H, m)

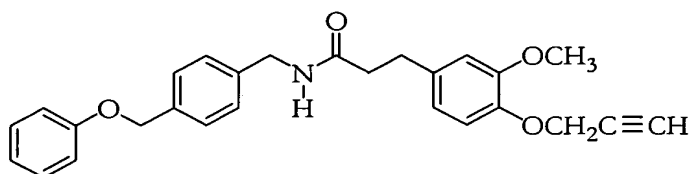
# 25 Production Example 113

52 mg of phenol, 5 ml of dimethylformamide and 24 mg of



55 % sodium hydride were mixed and stirred at room temperature for 15 minutes. 0.20 g of 4-((3-(3-methoxy-4-(2-propynyloxy)phenyl)propionyl)aminomethyl)benzyl methansulfonate was mixed with the reaction mixture and stirred at room temperature for 3 hours. Then ethyl acetate was added to the reaction mixture, and washed with 5 % hydrochloric acid, water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride. After that, it was dried by magnesium sulfate, and concentrated under reduced pressure. The obtained solid was purified by silica gel column to obtain 97 mg of N-(4-phenoxyethylbenzyl)-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide (referred as the compound of the present invention 113 hereinafter).

15 the compound of the present invention 113



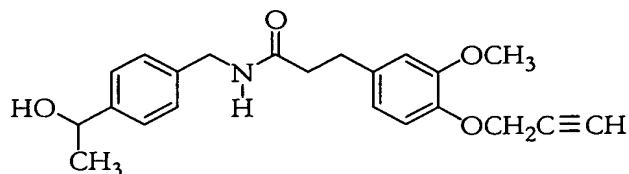
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.37 (2H, d,  $J=8.1$  Hz), 7.26-7.30 (2H, m), 7.17 (2H, d,  $J=8.1$  Hz), 6.93-6.99 (4H, m), 6.71-6.75 (2H, m), 5.57 (1H, br.s), 5.04 (2H, s), 4.73 (2H, d,  $J=2.4$  Hz), 4.41 (2H, d,  $J=5.6$  Hz), 3.82 (3H, s), 3.37 (3H, s), 2.95 (2H, t,  $J=7.5$  Hz), 2.47-2.52 (3H, m)

Production Example 114

By using 1.0 g of N-(4-methylcarbonylbenzyl)-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide, 0.06 g of sodium borohydride according to the Production Example 108 was obtained 1.0 g of

N-(4-(1-hydroxyethyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 114 hereinafter).

the compound of the present invention 114



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$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.29 (2H, d,  $J=8.1$  Hz), 7.12 (2H, d,  $J=8.1$  Hz), 6.93 (1H, d,  $J=8.5$  Hz), 6.69-6.71 (2H, m), 5.63 (1H, br.s), 4.87-4.88 (1H, m), 4.72 (2H, d,  $J=2.5$  Hz), 4.37 (2H, d,  $J=5.8$  Hz), 3.80 (3H, s), 2.94 (2H, t,  $J=7.5$  Hz), 2.47-2.53 (3H, m), 1.63 (1H, br.s), 1.47 (3H, d,  $J=6.5$  Hz)

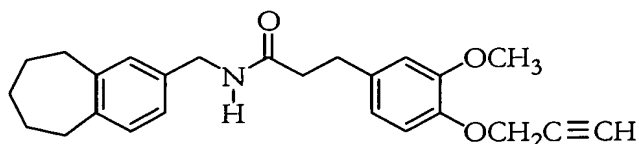
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Production Example 115

By using 0.30 g of C-(6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl)methylamine and 0.30 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid according to the Production Example 94 was obtained 0.34 g of N-((6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl)methyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 115 hereinafter).

20

the compound of the present invention 115



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.03 (1H, d,  $J=7.6$  Hz), 6.93-6.95 (2H, m), 6.88 (1H, dd,  $J=7.6$  Hz, 1.7 Hz), 6.72-6.76 (2H, m), 5.56 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.34 (2H, d,  $J=5.6$  Hz),

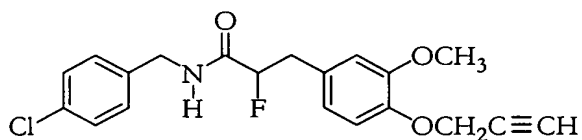
3.83 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.74-2.77 (4H, m), 2.46-2.50 (3H, m), 1.80-1.85 (2H, m), 1.59-1.65 (4H, m)

# Production Example 116

0.3 g of

5 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}-propionic acid, 0.15 ml of thionyl chloride and 5 ml of toluene were mixed, and stirred at 80 °C for 1 hour. After cooling to room temperature, it was concentrated under reduced pressure. The obtained residue was mixed to the mixture of 0.22 g of 4-chlorobenzylamine, 0.5 ml of triethylamine and tetrahydrofuran at 0 °C, and stirred at room temperature for 1 hour. Water and ethyl acetate were added to the reaction mixture, then organic layer was separated. The organic layer was washed with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained solid was washed by hexane to obtain 0.20 g of N-(4-chlorobenzyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 116 hereinafter).

the compound of the present invention 116



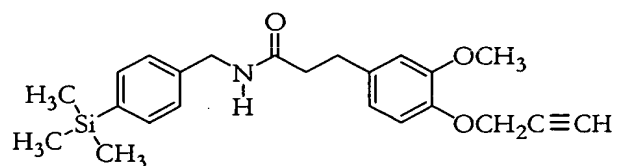
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.25 (2H, d, J=8.2 Hz), 6.93-6.98 (3H, m), 6.77-6.78 (2H, m), 6.44 (1H, br.s), 5.13 (1H, ddd, J=49 Hz, 6.1 Hz, 3.9 Hz), 4.76 (2H, d, J=2.4 Hz), 4.48 (1H, dd, J=15 Hz, 6.5 Hz), 4.26 (1H, dd, J=15 Hz, 5.3 Hz), 3.82 (3H, s), 3.28

(1H, ddd, J=26 Hz, 15 Hz, 3.9 Hz), 3.14 (1H, ddd, J=33 Hz, 15 Hz, 6.0 Hz), 2.50 (1H, t, J=2.4 Hz)

#### Production Example 117

By using 0.65 g of 4-trimethylsilylbenzylamine, 0.78 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-propionic acid according to the Production Example 94 was obtained 0.68 g of N-(4-trimethylsilylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 117 hereinafter).

the compound of the present invention 117

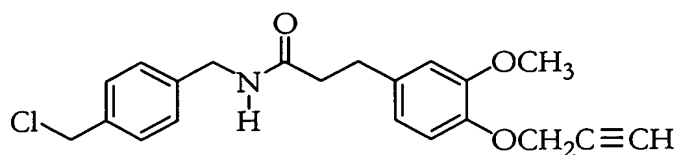


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.46 (2H, d, J=8.0 Hz), 7.16 (2H, d, J=8.0 Hz), 6.94 (1H, d, J=8.0 Hz), 6.71-6.76 (2H, m), 5.32 (1H, br.s), 4.73 (2H, d, J=2.4 Hz), 4.40 (2H, d, J=5.8 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.47-2.51 (3H, m), 0.26 (9H, s)

#### Production Example 118

By using 0.30 g of 4-((3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl)aminomethyl)-benzylmethansulfonate, 0.30 g of lithium chloride according to the Production Example 109 was obtained 0.25 g of N-(4-chloromethylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 118 hereinafter).

the compound of the present invention 118

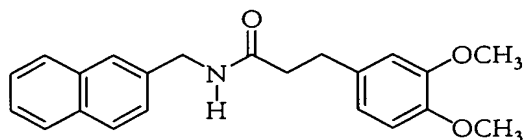


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.32 (2H, d, J=7.9 Hz), 7.13 (2H, d, J=7.9 Hz), 6.94 (1H, d, J=7.9 Hz), 6.71-6.75 (2H, m), 5.59 (1H, br.s), 4.74 (2H, d, J=2.4 Hz), 4.56 (2H, s), 4.40 (2H, d, J=5.9 Hz), 3.82 (3H, s), 2.95 (2H, t, J=7.3 Hz), 2.48-2.52 (3H, m)

#### Production Example 119

0.30 g of 3-(3,4-dimethoxyphenyl)propionyl chloride, 0.21 g of (naphthalene-2-yl)methylamine, 0.50 ml of triethylamine and 10 ml of tetrahydrofuran were mixed, and stirred at room temperature for 20 minutes. Then water was added to the reaction mixture, extracted with ethyl acetate. The organic layer was washed successively with 5% hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 0.25 g of N-((naphthalene-2-yl)methyl)-3-(3,4-dimethoxyphenyl)propanamide (referred as the compound of the present invention 119 hereinafter).

the compound of the present invention 119

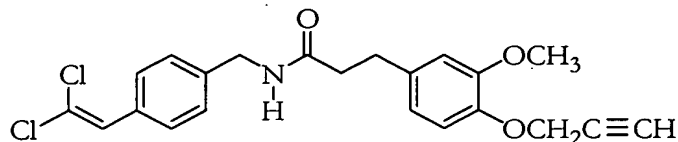


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.75-7.82 (3H, m), 7.60 (1H, s), 7.44-7.48 (2H, m), 7.25-7.28 (1H, m), 6.73-6.74 (3H, m), 5.66

(1H, br.s), 4.56 (2H, d, J=5.8 Hz), 3.82 (3H, s), 3.82 (3H, s),  
2.96 (2H, t, J=7.5 Hz), 2.53 (2H, t, J=7.5 Hz)

# Production Example 120

0.65 g of  
5 N-(4-formylbenzyl)-3-{3-methoxy-4-(2-propyonyl)phenyl}propanamide and 10 ml of methylenechloride were mixed, 1.5 g of triphenylphosphine and 2 ml of carbontetrachloride were mixed with it under ice cooling, followed by stirring under ice cooling for 2 hours and at room temperature for 15 hours. Then the reaction  
10 mixture was concentrated under reduced pressure. The obtained residue was purified by silica gel column twice to obtain 0.15 g of N-(4-(2,2-dichlorovinyl)benzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present  
15 invention 120 hereinafter).  
the compound of the present invention 120



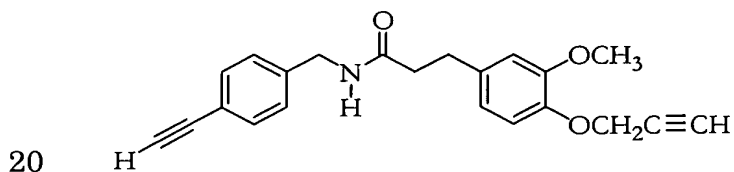
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.49 (0.8H, d, J=8.5 Hz), 7.46 (1.2H, d, J=8.2 Hz), 7.12-7.17 (2H, m), 6.93-6.95 (1H, m), 6.82 (0.6H, s), 6.71-6.75 (2H, m), 6.68 (0.4H, s), 5.62 (1H, br.s), 4.73-4.74 (2H, m), 4.39-4.42 (2H, m), 3.82 (3H, s), 2.95 (2H, t, J=7.5 Hz), 2.48-2.53 (3H, m)

# Production Example 121

0.52 g of 4-(trimethylsilylethynyl)benzylamine acetic  
25 acid salt, 0.42 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 0.38 g of

WSC and 10 ml of dimethylformamide were mixed at room temperature for 4 hours. Then water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. Obtained residue , 10 ml of methanol and 0.5 g of potassium carbonate were stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure. It was added water, and extracted with ethyl acetate. The organic layer was washed successively with water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column to obtain 0.21 g of N-(4-ethynylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 121 hereinafter).

the compound of the present invention 121



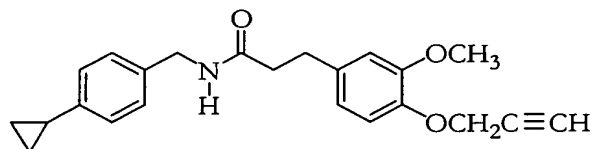
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.40-7.42 (2H, m), 7.09 (2H, d,  $J=8.3$  Hz), 6.93 (1H, d,  $J=8.3$  Hz), 6.70-6.75 (2H, m), 5.60 (1H, br.s), 4.74 (2H, d,  $J=2.4$  Hz), 4.39 (2H, d,  $J=5.9$  Hz), 3.82 (3H, s), 3.06 (1H, s), 2.95 (1H, t,  $J=7.5$  Hz), 2.47-2.59 (3H, m)

25 Production Example 122

0.51 g of 4-cyclopropylbenzylamine, 0.74 g of

3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 0.67 g of WSC and 10 ml of dimethylformamide were mixed at room temperature for 2 hours. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5% hydrochloric acid, water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was subjected to silica gel column to obtain 0.47 g of N-(4-cyclopropylbenzyl)-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 122 hereinafter).

the compound of the present invention 122



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.05 (2H, d,  $J=8.2$  Hz), 7.00 (2H, d,  $J=8.2$  Hz), 6.93 (1H, d,  $J=8.1$  Hz), 6.70-6.75 (2H, m), 5.59 (1H, br.s), 4.73 (2H, d,  $J=2.4$  Hz), 4.35 (2H, d,  $J=5.6$  Hz), 3.82 (3H, s), 2.94 (2H, t,  $J=7.3$  Hz), 2.46-2.49 (3H, m)

Production Example 123

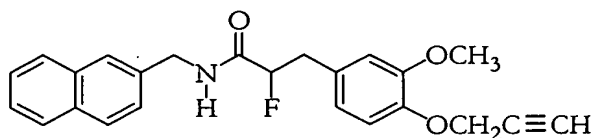
0.2 g of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 0.15 g of C-naphtalene-2-ylmethylamine hydrochloride, 0.19 g of WSC, 1 ml of pyridine and 5 ml of dimethylformamide were mixed at room temperature for 2 hours. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5% hydrochloric acid, water,



saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was subjected to silica gel column to obtain 0.13 g of

5 N-((naphthalene-2-yl)methyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 123 hereinafter).

the compound of the present invention 123



10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.76-7.82 (3H, m), 7.57 (1H, br.s), 7.46-7.56 (2H, m), 7.17 (1H, dd,  $J=8.2$  Hz, 1.7 Hz), 6.91 (1H, d, 8.7 Hz), 6.78-6.80 (2H, m), 6.50 (1H, br.s), 5.18 (1H, ddd,  $J=49$  Hz, 6.1 Hz, 3.6 Hz), 6.63-6.70 (3H, m), 4.49 (1H, dd,  $J=15$  Hz, 5.3 Hz), 3.80 (3H, s), 3.14-3.32 (2H, m), 2.47 (1H, t,  $J=2.4$  Hz)

15 Hz)

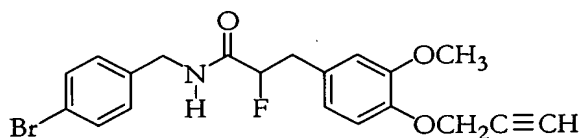
#### Production Example 124

0.5 g of crude product of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride, 0.49 g of 4-bromobenzylamine hydrochloride, 0.64 ml

20 of triethylamine, about 10 mg of dimethylaminopyridine and 10 ml of tetrahydrofuran were mixed at room temperature for 20 minutes. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5% hydrochloric acid, water, saturated aqueous solution of sodium

25 bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced

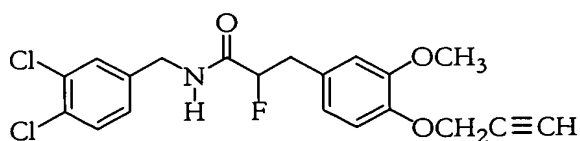
pressure. The residue was subjected to silica gel column to obtain 0.23 g of N-(4-bromobenzyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 124 hereinafter).  
the compound of the present invention 124



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.40 (2H, d, J=8.6 Hz), 6.94 (2H, d, J=8.6 Hz), 6.91 (1H, d, J=8.2 Hz), 6.77-6.78 (2H, m), 6.44 (1H, br.s), 5.16 (1H, ddd, J=49 Hz, 5.8 Hz, 3.6 Hz), 4.76 (2H, d, J=2.4 Hz), 4.47 (1H, dd, J=15 Hz, 6.8 Hz), 4.24 (1H, dd, J=15 Hz, 5.3 Hz), 3.82 (3H, s), 3.24 (1H, ddd, J=25 Hz, 15 Hz, 3.6 Hz), 3.14 (1H, ddd, J=34 Hz, 15 Hz, 5.8 Hz), 2.50 (1H, t, J=2.4 Hz)

#### 15 Production Example 125

By using 0.5 g of crude product of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.39 g of 3,4-dichlorobenzylamine according to the Production Example 124 was obtained 0.31 g of N-(3,4-dichlorobenzyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 125 hereinafter).  
the compound of the present invention 125

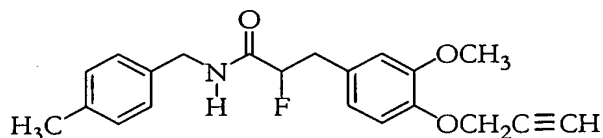


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.35 (1H, d, J=8.2 Hz), 7.25-2.26 (1H, m), 6.94 (1H, d, J=8.7 Hz), 6.83 (1H, dd, J=8.2 Hz, 2.2 Hz), 6.76-6.78 (2H, m), 6.49 (1H, br.s), 5.16 (1H, ddd, J=49 Hz, 6.1 Hz, 3.9 Hz), 4.75 (2H, d, J=2.4 Hz), 4.44 (1H, dd, J=15 Hz, 6.8 Hz), 4.27 (1H, dd, J=15 Hz, 5.5 Hz), 3.82 (3H, s), 3.28 (1H, ddd, J=26 Hz, 15 Hz, 3.9 Hz), 3.14 (1H, ddd, J=33 Hz, 15 Hz, 6.1 Hz), 2.49 (1H, t, J=2.4 Hz)

#### Production Example 126

By using 0.5 g of crude product of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.27 g of 4-methylbenzylamine according to the Production Example 124 was obtained 0.30 g of N-(4-methylbenzyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 126 hereinafter).

the compound of the present invention 126



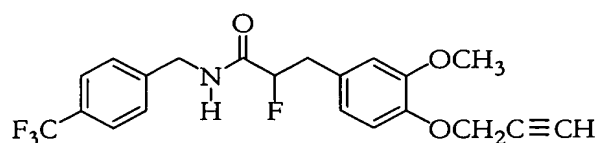
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.10 (2H, d, J=7.8 Hz), 6.94-6.98 (3H, m), 6.78-6.79 (2H, m), 6.39 (1H, br.s), 5.13 (1H, ddd, J=49 Hz, 6.4 Hz, 3.4 Hz), 4.75 (2H, d, J=2.4 Hz), 4.44 (1H, dd, J=15 Hz, 6.5 Hz), 4.24 (1H, dd, J=15 Hz, 5.3 Hz), 3.82 (3H, s), 3.28 (1H, ddd, J=27 Hz, 15 Hz, 3.4 Hz), 3.13 (1H, ddd, J=32 Hz, 15 Hz, 6.4 Hz), 2.49 (1H, t, J=2.4 Hz)

#### Production Example 127

By using 0.5 g of crude product of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl

chloride and 0.39 g of 4-trifluoromethylbenzylamine according to the Production Example 124 was obtained 0.29 g of N-(4-trifluoromethylbenzyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 127 hereinafter).

the compound of the present invention 127

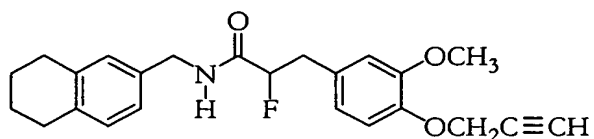


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.54 (2H, d,  $J=8.2$  Hz), 7.13 (2H, d,  $J=8.2$  Hz), 6.95 (1H, d,  $J=8.7$  Hz), 6.78-6.79 (2H, m), 6.52 (1H, br.s), 5.18 (1H, ddd,  $J=49$  Hz, 5.8 Hz, 3.8 Hz), 4.75 (2H, d,  $J=2.4$  Hz), 4.58 (1H, dd,  $J=15$  Hz, 6.8 Hz), 4.34 (1H, dd,  $J=15$  Hz, 5.3 Hz), 3.81 (3H, s), 3.09-3.35 (2H, m), 2.48 (1H, t,  $J=2.4$  Hz)

#### Production Example 128

By using 0.5 g of crude product of 2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride and 0.44 g of (5,6,7,8-tetrahydronaphthalene-2-yl)methylamine hydrochloride according to the Production Example 124 was obtained 0.33 g of N-((5,6,7,8-tetrahydronaphthalene-2-yl)methyl)-2-fluoro-3-{3-methoxy-4-(2-propynyloxy)phenyl}propanamide (referred as the compound of the present invention 128 hereinafter).

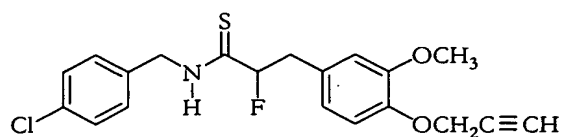
the compound of the present invention 128



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.00 (1H, d,  $J=7.8$  Hz), 6.95 (1H, d,  $J=8.7$  Hz), 6.78-6.85 (4H, m), 6.39 (1H, br.s), 5.12 (1H, ddd,  $J=49$  Hz, 6.5 Hz, 3.4 Hz), 4.74 (2H, d,  $J=2.4$  Hz), 4.28-4.39 (2H, m), 3.83 (3H, s), 3.28 (1H, ddd,  $J=28$  Hz, 15 Hz, 3.4 Hz), 3.12 (1H, ddd,  $J=31$  Hz, 15 Hz, 6.5 Hz), 2.75-2.80 (4H, m), 2.49 (1H, t,  $J=2.4$  Hz), 1.74-1.82 (4H, m)

Production Example 129

1.1 g of  
 10 N-(4-chlorobenzyl)-2-fluoro-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanamide, 0.86 g of Lawesson's Reagent and 30 ml of tetrahydrofuran were mixed, and stirred at 65 °C for 3 hours. Then the reaction mixture was cooled, and concentrated under reduced pressure. Water was added to the residue, and extracted  
 15 with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain  
 20 0.15 g of N-(4-chlorobenzyl)-2-fluoro-3-(3-methoxy-4-(2-propynyloxy)phenyl)propanthioamide (referred as the compound of the present invention 129 hereinafter).  
 the compound of the present invention 129



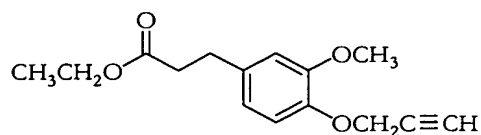
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.79 (1H, br.s), 7.24-7.29 (2H, m),  
 6.92-6.94 (3H, m), 6.78-6.80 (2H, m), 5.52 (1H, dt,  $J=50$  Hz,  
 4.5 Hz), 4.83 (1H, dd,  $J=15$  Hz, 6.1 Hz), 4.76 (2H, d, 2.4 Hz),  
 5 4.57 (1H, dd,  $J=15$  Hz, 4.8 Hz), 3.81 (3H, s), 3.27-3.51 (2H,  
 m), 2.50 (1H, t,  $J=2.4$  Hz)

Next, the production of the intermediate of the present invention is described as Reference Production Example.

#### 10 Reference Production Example 1

23.8 g of ethyl 3-(4-hydroxy-3-methoxyphenyl)propionate, 11.4 ml of propargyl bromide, 20.5 g of potassium carbonate and 250 ml of acetonitrile were mixed, and stirred at 80 °C for 2 hours. Then the reaction mixture was cooled to room temperature.

15 Ethyl acetate was added to it, and filtered. The filtrate was concentrated under reduced pressure to obtain 28.9 g of ethyl 3-(3-methoxy-4-(2-propynyloxy)phenyl)propionate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.95 (1H, d,  $J=7.7$  Hz), 6.72-6.75  
 20 (2H, m), 4.73 (2H, d,  $J=2.4$  Hz), 4.13 (2H, q,  $J=7.2$  Hz), 3.86  
 (3H, s), 2.90 (2H, t,  $J=7.5$  Hz), 2.60 (2H, t,  $J=7.5$  Hz), 2.49  
 (1H, t,  $J=2.4$  Hz), 1.24 (3H, t,  $J=7.0$  Hz)

#### Reference Production Example 2

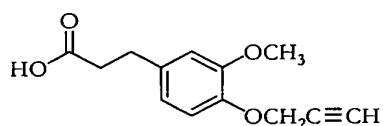
28.9

g

of

ethyl

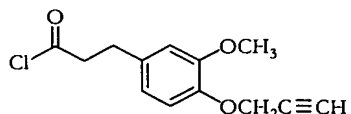
3-{3-methoxy-4-(2-propynyloxy)phenyl}propionate, 4.0 g of lithium hydroxide, 300 ml of tetrahydrofuran and 100 ml of water were mixed, and stirred at 65 °C for 3 hours. Then water was added to the reaction mixture, and concentrated under reduced pressure. 5 % hydrochloric acid was added to the residue and extracted with chloroform by three times. The organic layer was dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 22.7 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.96 (1H, d,  $J=8.2$  Hz), 6.73–6.75 (2H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.85 (3H, s), 2.91 (2H, t,  $J=8$  Hz), 2.67 (2H, t,  $J=8$  Hz), 2.49 (1H, t,  $J=2.4$  Hz)

Reference Production Example 3

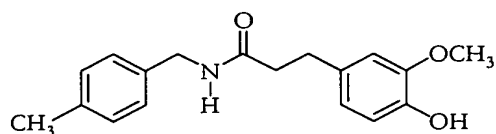
12.7 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid, 4.3 ml of thionyl chloride, 100 ml of toluene and about 0.05 g of N,N-dimethylformamide were mixed, and stirred at 80 °C for 30 minutes. Then the reaction mixture was cooled to room temperature, and concentrated under reduced pressure to obtain 14.6 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionyl chloride.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.97 (1H, d,  $J=8.8$  Hz), 6.72–6.74 (2H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.87 (3H, s), 3.19 (2H, t,  $J=7.2$  Hz), 2.99 (2H, t,  $J=7.2$  Hz), 2.49 (1H, t,  $J=2.4$  Hz)

## Reference Production Example 4

6.2 g of N-(4-methylbenzyl)-3-{3-methoxy-4-(benzyloxy)phenyl}acrylamide 0.6 g of 5 % palladium charcoal, 0.3 g of palladium hydroxide, 100 ml of ethanol, 100 ml of ethyl acetate, 100 ml of tetrahydrofuran and 1 ml of 36 % hydrochloric acid were stirred under hydrogen atmosphere. After stopping the absorption of hydrogen, the reaction mixture was filtered, and the filtrate was concentrated under reduced pressure. Ethyl acetate and water was added to the residue, and separated into two layer. The organic layer was dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 4.5 g of N-(4-methylbenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide



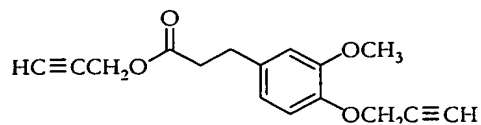
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.10 (2H, d,  $J=8$  Hz), 7.03 (2H, d,  $J=8$  Hz), 6.81 (1H, d,  $J=8.0$  Hz), 6.66-6.70 (2H, m), 5.78 (1H, br.s), 4.35 (2H, d,  $J=5.1$  Hz), 3.82 (3H, s), 2.92 (2H, d,  $J=7$  Hz), 2.47 (2H, d,  $J=7$  Hz), 2.32 (3H, s)

## Reference Production Example 5

50 g of 3-(4-hydroxy-3-methoxyphenyl)propionic acid, 50 ml of propargyl bromide, 88 g of potassium carbonate and 500 ml of acetonitrile were mixed, and stirred at 80 °C for 3 hours. Then the reaction mixture was cooled to room temperature. Ethyl acetate was added to it, and filtered. The filtrate was



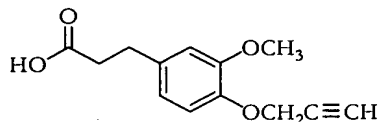
concentrated under reduced pressure to obtain 67 g of (2-propynyl)  
3-{3-methoxy-4-(2-propynyloxy)phenyl}propionate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.96 (1H, d, J=7.8 Hz), 6.68-6.75  
5 (2H, m), 4.73 (2H, d, J=2.2 Hz), 4.68 (2H, d, J=2.2 Hz), 3.87  
(3H, s), 2.93 (2H, t, J=7.3 Hz), 2.67 (2H, t, J=7.3 Hz), 2.47-2.50  
(2H, m)

Reference Production Example 6

67 g of (2-propynyl)  
10 3-{3-methoxy-4-(2-propynyloxy)phenyl}propionate, 8.08 g of  
lithium hydroxide, 400 ml of tetrahydrofuran and 200 ml of water  
were mixed, and stirred at 65 °C for 3 hours. Then water was  
added to the reaction mixture, and concentrated under reduced  
pressure. 5 % hydrochloric acid was added to the residue and  
15 extracted with chloroform by three times. The organic layer was  
dried by magnesium sulfate, and concentrated under reduced  
pressure. The residue was washed by hexane to obtain 51 g of  
3-{3-methoxy-4-(2-propynyloxy)phenyl}propionic acid.

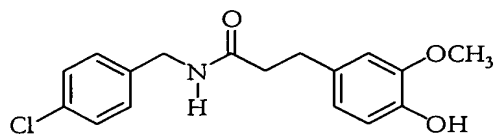


20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.96 (1H, d, J=8.2 Hz), 6.73-6.75  
(2H, m), 4.73 (2H, d, J=2.4 Hz), 3.85 (3H, s), 2.91 (2H, t, J=8  
Hz), 2.67 (2H, t, J=8 Hz), 2.49 (1H, t, J=2.4 Hz)

Reference Production Example 7

20.0 g of 3-(4-hydroxy-3-methoxyphenyl)propionic acid,

15 g of 4-chlorobenzylamine, 0.51 g of 2-nitrophenylboronic acid and 300 ml of toluene were mixed, and stirred under the condition of reflux and dehydration with Dean-Stark trap for 4 hours. Then the reaction mixture was cooled to room temperature, and added about 1000 ml of ethyl acetate. It was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was recrystallized from toluene to obtain 28 g of N-(4-chlorobenzyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide.

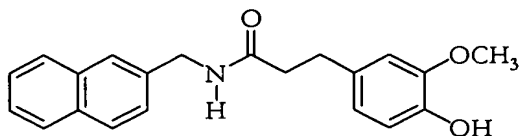


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.25 (2H, d, J=8.5 Hz), 7.03 (2H, d, J=8.5 Hz), 6.83 (1H, d, J=8.0 Hz), 6.66-6.69 (2H, m), 5.62 (1H, br.s), 5.53 (1H, s), 4.35 (2H, d, J=5.8 Hz), 3.82 (3H, s), 2.92 (2H, d, J=7.5 Hz), 2.49 (2H, d, J=7.5 Hz)

#### Reference Production Example 8

12.5 g of 3-(4-hydroxy-3-methoxyphenyl)propionic acid, 10.0 g of (C-naphthalene-2-yl)methylamine, 13.4 g of WSC and 100 ml of N,N-dimethylformamide were mixed, and stirred at room temperature for 2 hours. Then water was added to the reaction mixture and extracted with chloroform. The organic layer was washed successively with 5 % hydrochloric acid and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed

by hexane to obtain 15.1 g of N-(naphthalene-2-ylmethyl)-3-(4-hydroxy-3-methoxyphenyl)propanamide.

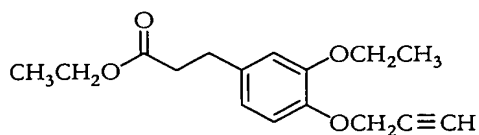


5  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.73-7.84 (3H, m), 7.58 (1H, s), 7.43-7.51 (2H, m), 7.23-7.27 (1H, m), 6.82 (1H, d,  $J=7.6$  Hz), 6.67-6.72 (2H, m), 5.67 (1H, br.s), 5.49 (1H, s), 4.56 (2H, d,  $J=5.9$  Hz), 3.77 (3H, s), 2.94 (2H, d,  $J=7.5$  Hz), 2.51 (2H, d,  $J=7.5$  Hz)

#### 10 Reference Production Example 9

16.2 g of ethyl 3-(4-hydroxy-3-ethoxyphenyl)propionate, 7.3 ml of propargyl bromide, 13.2 g of potassium carbonate and 160 ml of acetonitrile were mixed, and stirred at 80 °C for 2 hours. Then the reaction mixture was cooled to room temperature.

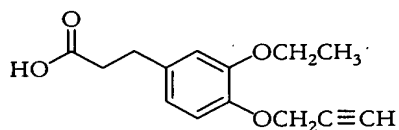
15 Ethyl acetate was added to it, and filtered. The filtrate was concentrated under reduced pressure to obtain 18.8 g of ethyl 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionate.



20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.96 (1H, d,  $J=8.0$  Hz), 6.74 (1H, d,  $J=1.9$  Hz), 6.72 (1H, dd,  $J=8.0$  Hz, 1.9 Hz), 4.73 (2H, d,  $J=2.4$  Hz), 4.12 (2H, q,  $J=7.0$  Hz), 4.07 (2H, q,  $J=7.0$  Hz), 2.89 (2H, t,  $J=7.5$  Hz), 2.59 (2H, t,  $J=7.5$  Hz), 2.48 (1H, t,  $J=2.4$  Hz), 1.44 (3H, t,  $J=7.0$  Hz), 1.23 (3H, t,  $J=7.0$  Hz)

#### Reference Production Example 10

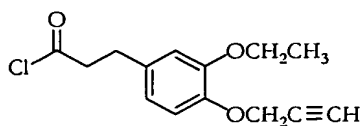
28.7 g of ethyl 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionate, 2.3 g of lithium hydroxide, 180 ml of tetrahydrofuran and 60 ml of water were mixed, and stirred at 65 °C for 3 hours. Then water was added to the reaction mixture, and concentrated under reduced pressure. The mixture was washed with methyl-tert-butyl ether and aqueous layer was separated. 5 % hydrochloric acid was added to the aqueous layer, and extracted with ethyl acetate. The organic layer was washed with saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 15.5 g of 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionic acid.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.97 (1H, d, J=8.2 Hz), 6.74 (1H, d, J=1.9 Hz), 6.73 (1H, dd, J=8.2 Hz, 1.9 Hz), 4.73 (2H, d, J=2.4 Hz), 4.08 (2H, q, J=7.0 Hz), 2.90 (2H, t, J=7.7 Hz), 2.66 (2H, t, J=7.7 Hz), 2.48 (1H, t, J=2.4 Hz), 1.44 (3H, t, J=7.0 Hz)

Reference Production Example 11

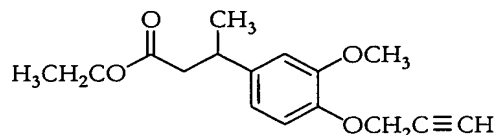
6.7 g of 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionic acid, 3.2 ml of thionyl chloride, 100 ml of toluene and about 0.03 g of N,N-dimethylformamide were mixed, and stirred at 80 °C for 30 minutes followed by at 100 °C for 30 minutes. Then the reaction mixture was cooled to room temperature, and concentrated under reduced pressure to obtain 17.5 g of 3-{3-ethoxy-4-(2-propynyloxy)phenyl}propionyl chloride.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.98 (1H, d,  $J=8.3$  Hz), 6.71-6.73 (2H, m), 4.74 (2H, d,  $J=2.4$  Hz), 4.08 (2H, q,  $J=7.1$  Hz), 3.18 (2H, t,  $J=7.6$  Hz), 2.95 (2H, t,  $J=7.6$  Hz), 2.49 (1H, t,  $J=2.4$  Hz), 1.45 (3H, t,  $J=7.1$  Hz)

#### Reference Production Example 12

7.14 g of ethyl 3-(4-hydroxy-3-methoxyphenyl)butyrate, 3.93 g of 3-bromopropyn, 4.98 g of potassium carbonate and 50 ml of acetonitrile were mixed, and stirred at 80 °C for 4 hours. Then the reaction mixture was cooled to room temperature, water was added to it, and extracted with ethyl acetate. The organic layer was washed successively with water and aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure to obtain 8.3 g of ethyl 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyrate.

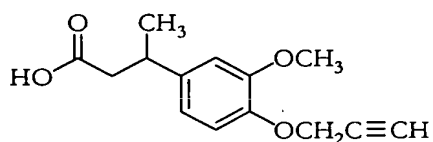


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.96 (1H, d,  $J=8.9$  Hz), 6.73-6.78 (2H, m), 4.72 (2H, d,  $J=2.4$  Hz), 4.08 (2H, q,  $J=7.0$  Hz), 3.86 (3H, s), 3.18-3.29 (1H, m), 2.47-2.63 (3H, m), 1.28 (3H, d,  $J=7.0$  Hz), 1.19 (3H, t,  $J=7.1$  Hz)

#### Reference Production Example 13

8.0 g of ethyl 3-(3-methoxy-4-(2-propynyloxy)phenyl)butyrate 1.04 g of lithium hydroxide, 40 ml of tetrahydrofuran and 15 ml of water

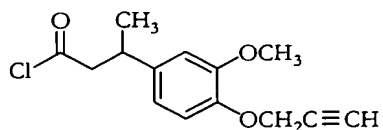
were mixed, and stirred at 65 °C for 4 hours. Then water was added to the reaction mixture and concentrated under reduced pressure. 5 % hydrochloric acid was added to the residue, and extracted with chloroform by three times. The organic layer was washed with successively water and saturated aqueous solution of sodium chloride. The organic layer was dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 7.0 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyric acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.97 (1H, d,  $J=8.8$  Hz), 6.74-6.78 (2H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.86 (3H, s), 3.17-3.30 (1H, m), 2.52-2.70 (2H, m), 2.49 (1H, t,  $J=2.4$  Hz), 1.31 (3H, d,  $J=7.1$  Hz)

#### Reference Production Example 14

7.0 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyric acid, 5.0 g of thionyl chloride and 100 ml of toluene were mixed, and stirred at 50 °C for 30 minutes followed by at 80 °C for 3 hours. Then the reaction mixture was cooled to room temperature, and concentrated under reduced pressure. The residue was washed by hexane to obtain 6.3 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}butyryl chloride.

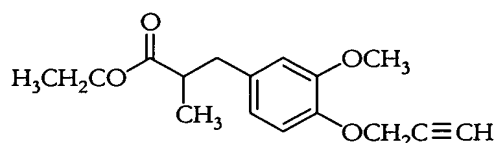


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.97 (1H, d,  $J=7.7$  Hz), 6.72-6.78

(2H, m), 4.73 (2H, d, J=2.4 Hz), 3.87 (3H, s), 3.25-3.35 (1H, m), 3.04-3.21 (2H, m), 2.49 (1H, t, J=2.4 Hz), 1.34 (3H, d, J=7.0 Hz)

#### Reference Production Example 15

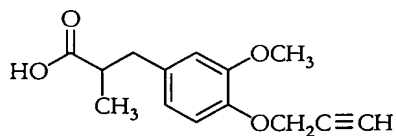
5 By using 5.93 g of ethyl 3-(3-methoxy-4-hydroxyphenyl)-2-methylpropionate according to Reference Production Example 12 was obtained 6.84 g of ethyl 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-methylpropionate.



10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.94 (1H, d, J=8.8 Hz), 6.68-6.74 (2H, m), 4.73 (2H, d, J=2.4 Hz), 4.09 (2H, q, J=7.0 Hz), 3.85 (3H, s), 2.92-3.01 (1H, m), 2.58-2.74 (2H, m), 2.48 (1H, t, J=2.4 Hz), 1.19 (3H, t, J=7.2 Hz), 1.15 (3H, d, J=6.8 Hz)

#### Reference Production Example 16

15 By using 6.50 g of ethyl 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-methylpropionate according to Reference Production Example 13 was obtained 5.33 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-methylpropionic acid.

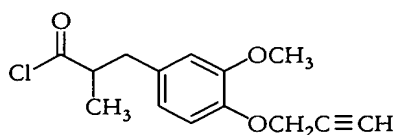


20

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.95 (1H, d, J=8.7 Hz), 6.70-6.75 (2H, m), 4.73 (2H, d, J=2.2 Hz), 3.84 (3H, s), 2.97-3.06 (1H, m), 2.58-2.80 (2H, m), 2.49 (1H, t, J=2.4 Hz), 1.19 (3H, d, J=6.7 Hz)

## Reference Production Example 17

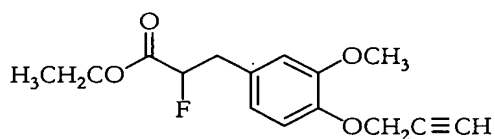
By using 5.03 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-methylpropionic acid according to Reference Production Example 14 was obtained 5.09 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-methylpropionyl chloride.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.96 (1H, d,  $J=8.2$  Hz), 6.72-6.75 (2H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.85 (3H, s), 3.07-3.18 (2H, m), 2.67-2.77 (1H, m), 2.49 (1H, t,  $J=2.4$  Hz), 1.28 (3H, d,  $J=6.8$  Hz)

## Reference Production Example 18

By using 2.0 g of crude product of ethyl 3-(3-methoxy-4-hydroxyphenyl)-2-fluoropropionate and 0.86 ml of 3-bromopropyne according to Reference Production Example 12 was obtained 2.3 g of crude product of ethyl 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-fluoropropionate.



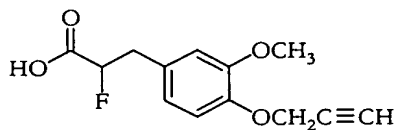
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.97 (1H, d,  $J=8.9$  Hz), 6.72-6.79 (2H, m), 5.06 (1H, ddd,  $J=49$  Hz, 7.5 Hz, 4.1 Hz), 4.74 (1H, d,  $J=2.4$  Hz), 4.23 (2H, q,  $J=7.0$  Hz), 3.86 (3H, s), 3.08-3.20 (2H, m), 2.49-2.50 (1H, m), 1.27 (3H, t,  $J=7.0$  Hz)

## Reference Production Example 19

By using 2.3 g of crude product of ethyl



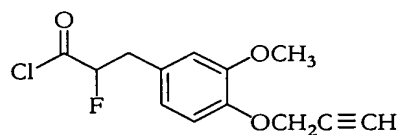
3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-fluoropropionate according to Reference Production Example 13 was obtained 1.8 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-fluoropropionic acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.98 (1H, d,  $J=8.7$  Hz), 6.74-6.82 (2H, m), 5.21 (1H, ddd,  $J=49$  Hz, 7.5 Hz, 3.6 Hz), 4.75 (1H, d,  $J=2.4$  Hz), 3.86 (3H, s), 3.08-3.31 (2H, m), 2.49 (1H, t,  $J=2.4$  Hz)

10 Reference Production Example 20

By using about 4.7 g of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-fluoropropionic acid according to Reference Production Example 14 was obtained 5.0 g crude product of 3-{3-methoxy-4-(2-propynyloxy)phenyl}-2-fluoropropionyl chloride.

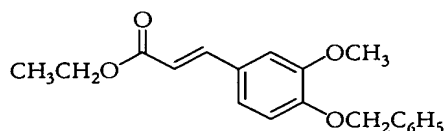


20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.99 (1H, d,  $J=8.2$  Hz), 6.79-6.82 (2H, m), 5.20 (1H, ddd,  $J=49$  Hz, 7.3 Hz, 3.9 Hz), 4.75 (2H, d,  $J=2.4$  Hz), 3.87 (3H, s), 3.17-3.37 (2H, m), 2.50 (1H, t,  $J=2.4$  Hz)

Next, the production of the intermediate is described as Reference Example.

## Reference Example 1

100 g of 4-benzyloxy-3-methoxybenzaldehyde, 120 g of ethyl diethylphosphonoacetate, 570 g of potassium carbonate and 570 ml of water were mixed, and stirred under condition of reflux for 20 hours. Then the reaction mixture was cooled to room temperature, water was added to it and extracted ethyl acetate twice. The separated organic layer was washed successively with water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was recrystallized from ethanol to obtain 58.6 g of ethyl 3-(3-methoxy-4-(benzyloxy)phenyl)acrylate.

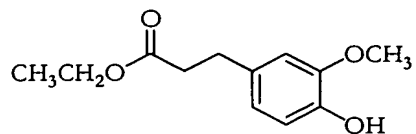


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.60 (1H, d,  $J=15$  Hz), 7.29-7.44 (5H, m), 7.06 (1H, d,  $J=1.9$  Hz), 7.02 (1H, dd,  $J=8.2$  Hz, 1.9 Hz), 6.86 (1H, d,  $J=8.2$  Hz), 6.29 (1H, d,  $J=15$  Hz), 5.18 (2H, s), 4.25 (2H, q,  $J=7.3$  Hz), 3.91 (3H, s), 1.33 (3H, t,  $J=7.3$  Hz)

## Reference Example 2

33 g of ethyl 3-(3-methoxy-4-(benzyloxy)phenyl)acrylate, 0.3 g of 5 % palladium charcoal, about 0.05 g of 36 % hydrochloric acid and 200 ml of ethanol were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure. Ethyl acetate and water were added to the residue and separated to two layer. The organic layer was dried by magnesium sulfate, added about 5 g of active carbon and about 5 g of caustic clay,

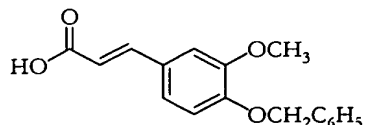
filtered, and concentrated under reduced pressure. The residue was washed by hexane to obtain 23 g of ethyl 3-(4-hydroxy-3-methoxyphenyl)propionate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.82 (1H, d, J=7.7 Hz), 6.67-6.70 (2H, m), 5.47 (1H, s), 4.19 (2H, q, J=7.2 Hz), 3.87 (3H, s), 2.88 (2H, t, J=7.5 Hz), 2.58 (2H, t, J=7.5 Hz), 1.24 (3H, t, J=7.2 Hz)

#### Reference Example 3

To 10 g of ethyl 3-{3-methoxy-4-(benzyloxy)phenyl}acrylate and 10 g of 20 % aqueous solution of sodium hydroxide, ethanol was mixed until it was homogenized. The obtained mixture was stirred under reflux for 2 hours. The reaction mixture was cooled, ethanol was distilled off under reduced pressure. Water was added to it, then adjusted to PH=2 with 5 % hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with saturated aqueous solution of sodium chloride twice, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 9 g of 3-{3-methoxy-4-(benzyloxy)phenyl}acrylic acid.

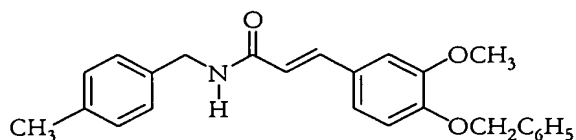


<sup>1</sup>H-NMR (CD<sub>3</sub>SOCD<sub>3</sub>, TMS) δ (ppm): 12.18 (1H, s), 7.51 (1H, d, J=16 Hz), 7.33-7.44 (6H, m), 7.05 (1H, d, J=8.2 Hz), 6.44 (1H, d,

$J=16$  Hz), 6.66-6.70 (2H, m), 5.13 (2H, s), 3.82 (3H, s)

#### Reference Example 4

5.0 g of 3-{3-methoxy-4-(benzyloxy)phenyl}acrylic acid, 2 ml of thionyl chloride, 100 ml of toluene and about 0.05 g of N,N-dimethylformamide were mixed and stirred at 80 °C for 30 minutes. Then the reaction mixture was cooled to room temperature, and concentrated under reduced pressure to obtain 3-{3-methoxy-4-(benzyloxy)phenyl}acrylic chloride. The 3-{3-methoxy-4-(benzyloxy)phenyl}-acrylic chloride, 2.1 g of 4-methylbenzylamine, 3.7 ml of triethylamine and 100 ml of tetrahydrofuran were mixed, and stirred at room temperature for 1 hour. Then water was added to the reaction mixture, solvent was distilled off under reduced pressure. The obtained solid was collected by filtration. The solid was washed by hexane, and dried to obtain 6.5 g of N-(4-methylbenzyl)-3-{3-methoxy-4-(benzyloxy)phenyl}acrylamide.

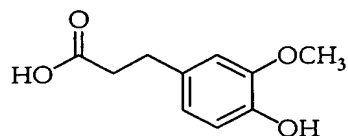


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.58 (1H, d,  $J=15$  Hz), 7.14-7.43 (9H, m), 6.98-6.99 (2H, m), 6.85 (1H, d,  $J=8.2$  Hz), 6.25 (1H, d,  $J=15$  Hz), 5.75 (1H, br.s), 5.75 (2H, s), 4.52 (2H, d,  $J=5.6$  Hz), 3.90 (3H, s), 2.34 (3H, s)

#### Reference Example 5

50 g of 3-(4-hydroxy-3-methoxyphenyl)acrylic acid, 0.5 g of 5 % of palladium charcoal, about 0.05 g of 36 % hydrochloric acid, 250 ml of ethanol and 100 ml of tetrahydrofuran were stirred

under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure to obtain 52 g of 3-(4-hydroxy-3-methoxyphenyl)propionic acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.83 (1H, dd,  $J=7.3$  Hz, 0.8 Hz), 6.81-6.70 (2H, m), 3.86 (3H, s), 2.88 (2H, t,  $J=7.6$  Hz), 2.65 (2H, t,  $J=7.6$  Hz)

#### Reference Example 6

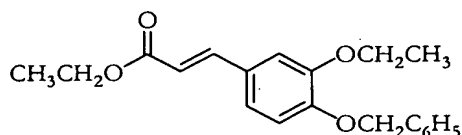
10            25 g of 3-ethoxy-4-hydroxybenzaldehyde, 27 g of benzyl bromide, 25 g of potassium carbonate and 250 ml of acetonitrile were mixed, and stirred under condition of reflux for 3 hours. Then the reaction mixture was cooled to room temperature. Ethyl acetate was added to it, and solid was filtered off. The obtained  
15 organic layer was concentrated under reduced pressure, the residue was washed by methyl-tert-butylether and hexane to obtain 36 g of 4-benzyloxy-3-ethoxybenzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 9.82 (1H, s), 7.28-7.44 (7H, m), 6.98 (1H, d,  $J=8.2$  Hz), 5.24 (2H, s), 4.18 (2H, q,  $J=7.0$  Hz),  
20 1.49 (3H, t,  $J=7.0$  Hz)

#### Reference Example 7

19 g of ethyl diethylphosphonoacetate and 400 ml of tetrahydrofuran were mixed, added 3.3 g of sodium hydride (content 60 %) under ice cooling, and stirred for 10 minutes. Then the  
25 mixture of 20 g of 4-benzyloxy-3-ethoxybenzaldehyde and 50 ml of tetrahydrofuran was added gradually to it under ice cooling,

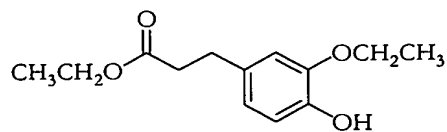
and stirred at room temperature for 1 hour. Water was added to the obtained mixture. Organic solvent was distilled off under reduced pressure, and then extracted with ethyl acetate. The oil layer was separated. It was washed with water, buffer solution of PH 6.8 and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 25 g of ethyl 3-{3-ethoxy-4-(benzyloxy)phenyl}acrylate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.59 (1H, d, J=16 Hz), 7.28-7.44 (5H, m), 7.07 (1H, d, J=2.0 Hz), 7.02 (1H, dd, J=8.3 Hz, 2.0 Hz), 6.86 (1H, d, J=8.3 Hz), 6.28 (1H, d, J=16 Hz), 5.18 (2H, s), 4.28 (2H, q, J=7.1 Hz), 4.31 (2H, q, J=6.8 Hz), 1.47 (3H, t, J=6.8 Hz), 1.33 (3H, t, J=7.1 Hz)

#### Reference Example 8

23 g of ethyl 3-{3-ethoxy-4-(benzyloxy)phenyl}acrylate, 0.2 g of 5 % palladium charcoal, about 0.04 g of 36 % hydrochloric acid, 120 ml of ethanol and 100 ml of tetrahydrofuran were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure. The residue was washed by hexane to obtain 17 g of ethyl 3-(4-hydroxy-3-ethoxyphenyl)propionate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.83 (1H, d, J=8.0 Hz), 6.66-6.70

(2H, m), 5.55 (1H, s), 4.01-4.15 (4H, m), 2.86 (2H, t, J=7.8 Hz), 2.57 (2H, t, J=7.8 Hz), 1.43 (3H, t, J=6.9 Hz), 1.23 (3H, t, J=7.2 Hz)

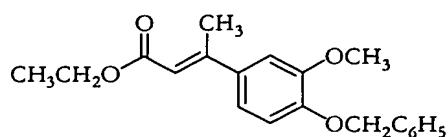
#### Reference Example 9

5           30 g of 4-acetyl-2-methoxyphenol, 32 g of benzyl bromide, 28 g of potassium carbonate and 300 ml of acetonitrile were mixed and stirred under condition of reflux for 4 hours. Then the reaction mixture was cooled to room temperature. Ethyl acetate was added to it, and the solid was filtered off. The obtained  
10       organic layer was concentrated under reduced pressure. The residue was washed by hexane to obtain 46 g of 4-benzyloxy-3-methoxyacetophenone.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.28-7.57 (7H, m), 6.89 (1H, d, J=8.3 Hz), 5.23 (2H, s), 3.94 (3H, s), 2.54 (3H, s)

#### 15       Reference Example 10

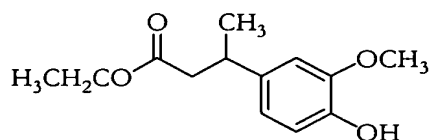
          18 g of ethyl diethylphosphonoacetate and 400 ml of tetrahydrofuran were mixed, added 3.2 g of sodium hydride (content 60 %) under ice cooling, and stirred for 10 minutes. Then the mixture of 20 g of 4-benzyloxy-3-methoxyacetophenone and 50 ml  
20       of tetrahydrofuran was added gradually to it under ice cooling, and stirred at room temperature for 2 hours. Water was added to the obtained mixture. The organic solvent was distilled off under reduced pressure, and then extracted with ethyl acetate. The oil layer was separated. It was washed with water and  
25       saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was purified by silica gel column to obtain 17 g of ethyl 3-(3-methoxy-4-benzyloxyphenyl)-2-butenate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.22-7.44 (5H, m), 7.00-7.02 (2H, m), 6.86 (1H, d,  $J=8.7$  Hz), 6.09 (1H, q,  $J=1.2$  Hz), 5.17 (2H, s), 4.21 (2H, q,  $J=7.0$  Hz), 3.92 (3H, s), 2.55 (3H, d,  $J=1.2$  Hz), 1.31 (3H, t,  $J=7.0$  Hz)

#### Reference Example 11

10.0 g of ethyl 3-{4-benzyloxy-3-methoxy-phenyl}-2-buten-2-ylideneacetate, 1.0 g of 10 % palladium charcoal, 15 ml of concentrated hydrochloric acid, 0.5 g of 10 % platinum charcoal and 100 ml of ethanol were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated with ethyl acetate to obtain 7.24 g of ethyl 3-(4-hydroxy-3-methoxyphenyl)butyrate.



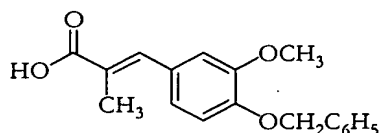
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.83 (1H, d,  $J=8.7$  Hz), 6.70-6.75 (2H, m), 5.50 (1H, br.s), 4.07 (2H, q,  $J=7.0$  Hz), 3.87 (3H, s), 3.15-3.26 (1H, m), 2.46-2.63 (2H, m), 1.27 (3H, d,  $J=6.7$  Hz), 1.19 (3H, t,  $J=7.0$  Hz)

#### Reference Example 12

30 g of 4-benzyloxy-3-methoxybenzaldehyde, 12 g of sodium propionate and 24 g of propionyl anhydride were mixed, and stirred at 150 °C for 6 hours. Then the reaction mixture was cooled to



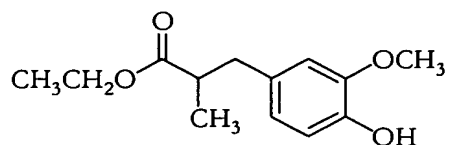
room temperature. Water was added to it and extracted with ethyl acetate. The oil layer was separated. It was washed with 5 % hydrochloric acid and saturated aqueous solution of sodium chloride twice, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was washed by toluene and hexane to obtain 28 g of 3-(3-methoxy-4-benzyloxyphenyl)-2-methylacrylic acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.74 (1H, br.s), 7.29-7.45 (5H, m), 6.99-7.04 (2H, m), 6.91 (1H, d,  $J=8.9$  Hz), 5.20 (2H, s), 3.91 (3H, s), 2.16 (3H, d,  $J=1.3$  Hz)

#### Reference Example 13

9 ml of acetyl chloride was mixed to 75 ml of ethanol, and stirred at room temperature for 10 minutes. 8.3 g of 3-(3-methoxy-4-benzyloxyphenyl)-2-methylacrylic acid was mixed to the said mixture, and stirred under the condition of reflux for 2 hours. The obtained reaction mixture was filtered, concentrated under reduced pressure. The residue, 1.0 g of 10 % palladium charcoal, 0.5 g of platinum charcoal, 15 ml of 36 % hydrochloric acid and 80 ml of ethanol were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure. The residue was washed by hexane to obtain 5.4 g of ethyl 3-(4-hydroxy-3-methoxyphenyl)-2-methyl-proionate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.81 (1H, d,  $J=8.5$  Hz), 6.64–6.66 (2H, m), 5.46 (1H, br.s), 4.09 (3H, q,  $J=7.1$  Hz), 3.86 (3H, s), 2.94 (1H, dd,  $J=13.3$  Hz, 6.8 Hz), 2.56–2.72 (2H, m), 1.20 (3H, t,  $J=7.1$  Hz), 1.14 (3H, d,  $J=7.0$  Hz)

#### Reference Example 14

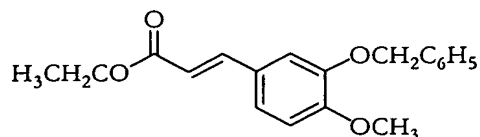
15.2 g of 3-hydroxy-4-methoxy-benzaldehyde, 18.0 g of benzyl bromide, 15.2 g of potassium carbonate and 200 ml of acetonitrile were mixed and stirred at 80 °C for 3 hours. Then the reaction mixture was cooled to room temperature, ethyl acetate was added to it and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column to obtain 23.3 g of (3-benzyloxy-4-methoxy)benzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 9.80 (1H, s), 7.30–7.48 (7H, m), 6.98 (1H, d,  $J=8.7$  Hz), 5.118 (2H, s), 3.95 (3H, s)

#### Reference Example 15

2.1 g of sodium hydride and 150 ml of tetrahydrofuran were mixed at 0 to 5 °C, and 11.2 g of ethyl diethylphosphonoacetate was dropped slowly to it. After dropping, it was stirred for 30 minutes. Then tetrahydrofuran solution of 12.1 g of (3-benzyloxy-4-methoxy)benzaldehyde was dropped, and stirred at 0 to 5 °C for 15 minutes then at room temperature for 30 minutes. After that, water was added to it and separated to two layer with ethyl acetate. The organic layer was dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 14.1 g of ethyl

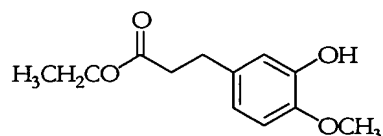
3-(3-benzyloxy-4-methoxyphenyl)acrylate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.56 (1H, d, J=15.7 Hz), 7.42-7.47 (2H, m), 7.34-7.41 (2H, m), 7.27-7.34 (1H, m), 7.11 (1H, dd, J=8.2 Hz, 1.9 Hz), 7.07 (1H, d, J=1.9 Hz), 6.87 (1H, d, J=8.2 Hz), 6.22 (1H, d, J=15.6 Hz), 5.15 (2H, s), 4.24 (2H, q, J=7.0 Hz), 3.91 (3H, s), 1.32 (3H, t, J=7.0 Hz)

Reference Example 16

8.0 g of ethyl 3-(3-benzyloxy-4-methoxyphenyl)acrylate, 0.8 g of 10 % palladium charcoal and 80 ml of ethanol were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure. The residue was washed by hexane to obtain 5.33 g of ethyl 3-(3-hydroxy-4-methoxyphenyl)proionate.

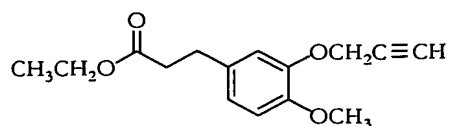


15

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.74-6.78 (2H, m), 6.67 (1H, dd, J=8.1 Hz, 2.0 Hz), 5.55 (1H, br.s), 4.12 (2H, q, J=7.0 Hz), 3.86 (3H, s), 2.85 (2H, t, J=7.9 Hz), 2.57 (2H, t, J=7.9 Hz), 1.23 (3H, t, J=7.1 Hz)

20 Reference Example 17

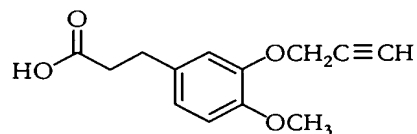
In the same way as in the Reference Production Example 12, 2.53 g of ethyl 3-(4-methoxy-3-(2-propynyloxy)phenyl)propionate was obtained from 2.24 g of ethyl 3-(3-hydroxy-4-methoxyphenyl)propionate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.79–6.89 (3H, m), 4.74 (2H, d,  $J=2.4$  Hz), 4.12 (2H, q,  $J=7.1$  Hz), 3.84 (3H, s), 2.89 (2H, t,  $J=7.6$  Hz), 2.59 (2H, t,  $J=7.6$  Hz), 2.49 (1H, t,  $J=2.4$  Hz), 1.24 (3H, t,  $J=7.1$  Hz)

#### Reference Example 18

In the same way as in the Reference Production Example 13, 1.93 g of 3-(4-methoxy-3-(2-propynyloxy)phenyl)propionic acid was obtained from 2.53 g of ethyl 3-(4-methoxy-3-(2-propynyloxy)phenyl)propionate.

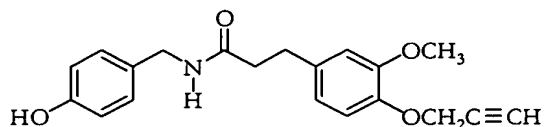


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.80–6.90 (3H, m), 4.75 (2H, d,  $J=2.4$  Hz), 3.84 (3H, s), 2.91 (2H, t,  $J=7.6$  Hz), 2.66 (2H, t,  $J=7.6$  Hz), 2.49 (1H, t,  $J=2.4$  Hz)

#### Reference Example 19

1.59 g of 4-hydroxy-benzylamine hydrochloride, 2.34 g of 3-(3-methoxy-4-(2-propynyloxy)phenyl)-propionic acid, 2.11 g of WSC and 25 ml of pyridine were mixed, and stirred at room temperature for 4 hours. Then water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed successively with 5 % hydrochloric acid, water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column to obtain 2.1 g of

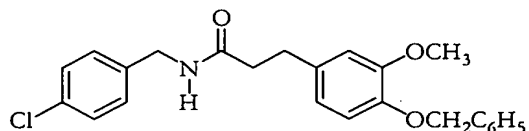
N-(4-hydroxy-benzyl)-3-{4-methoxy-3-(2-propynyloxy)phenyl}propanamide.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.91-7.02 (3H, m), 6.70-6.77 (4H, m), 5.54 (1H, br.s), 4.73 (2H, d, J=2.0 Hz), 4.31 (2H, d, J=5.6 Hz), 3.81 (3H, s), 2.94 (2H, t, J=7.6 Hz), 2.45-2.52 (3H, m)

Reference Example 20

10  
N-(4-chlorobenzyl)-3-{4-hydroxy-3-methoxyphenyl}propanamide,  
5.6 g of benzyl bromide, 5.6 g of potassium carbonate and 150  
10 ml of acetonitrile were mixed, and stirred under the condition  
of reflux for 4 hours. Then the reaction mixture was cooled to  
room temperature. Ethyl acetate was added to it, and the solid  
was filtered off. The obtained organic layer was concentrated  
15 under reduced pressure, the residue was washed by hexane to obtain  
11 g of  
N-(4-chlorobenzyl)-3-{4-benzyloxy-3-methoxyphenyl}propanami  
de.



20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.43-7.45 (2H, m), 7.23-7.38 (5H, m), 7.06 (2H, d, J=8.2 Hz), 6.78 (1H, d, J=8.0 Hz), 6.74 (1H, d, J=1.9 Hz), 6.64 (1H, dd, J=8.0 Hz, 1.9 Hz), 5.89 (1H, br.s), 5.12 (2H, s), 4.35 (2H, d, J=6.1 Hz), 3.84 (3H, s), 2.99 (2H, t, J=7.5 Hz), 2.49 (2H, t, J=7.5 Hz)

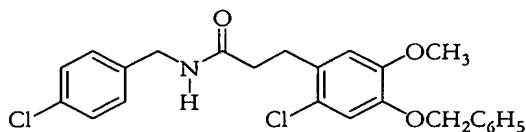
## Reference Example 21

3.7

g

of

N-(4-chlorobenzyl)-3-{4-benzyloxy-3-methoxyphenyl}propanamide, 50 ml of monochlorobenzene and 0.75 g 150 ml of sulfuric chloride were mixed, and stirred at room temperature for 1 hour. Then toluene was added to the reaction mixture, and solid was filtered off. The obtained solid was washed with toluene and hexane, and purified by silica gel column to obtain 3.3 g of N-(4-chlorobenzyl)-3-{4-benzyloxy-2-chloro-5-methoxyphenyl}propanamide.



$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.40 (1H, t,  $J=5.9$  Hz), 7.13–7.45 (9H, m), 7.07 (1H, s), 6.91 (1H, s), 5.08 (2H, s), 4.24 (2H, d,  $J=6.1$  Hz), 3.70 (3H, s), 2.81 (2H, t,  $J=7.5$  Hz), 2.44 (2H, t,  $J=7.5$  Hz)

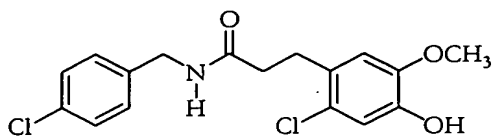
## Reference Example 22

3.0

g

of

N-(4-chlorobenzyl)-3-{benzyloxy-2-chloro-5-methoxyphenyl}propanamide, 50 ml of acetic acid and 1.48 g of 48 % hydrobromic acid were mixed and stirred at  $80^\circ\text{C}$  for 3 hours. Then the reaction mixture was concentrated under reduced pressure and purified by silica gel column to obtain 2.2 g of N-(4-chlorobenzyl)-3-{2-chloro-4-hydroxy-5-methoxyphenyl}propanamide.

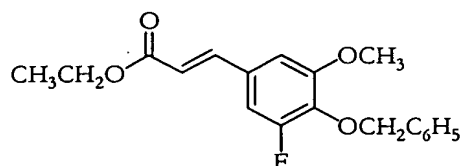


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.20-7.25 (2H, m), 7.00-7.04 (2H, m), 6.91 (1H, s), 6.71 (1H, s), 5.69 (1H, br.s), 5.62 (1H, s), 4.34 (2H, d,  $J=5.8$  Hz), 3.78 (3H, s), 3.01 (2H, t,  $J=7.2$  Hz), 2.51 (2H, t,  $J=7.2$  Hz)

#### Reference Example 23

1.1 g of 3-fluoro-4-hydroxy-5-methoxybenzaldehyde, 1.2 g of benzyl bromide, 1.3 g of potassium carbonate and 15 ml of acetonitrile were mixed, and stirred under the condition of reflux for 4 hours. Then the reaction mixture was cooled to room temperature. Ethyl acetate was added to it, and the solid was filtered off. The obtained organic layer was concentrated under reduced pressure, the residue was washed by hexane to obtain 1.8 g of 4-benzyloxy-3-fluoro-5-methoxybenzaldehyde. Next, 1.5 g of ethyl diethylphosphonoacetate and 20 ml of tetrahydrofuran were mixed. 0.29 g of sodium hydride (content 55%) was mixed to the mixture under ice cooling for 10 minutes. The mixture of 1.8 g of 4-benzyloxy-3-fluoro-5-methoxybenzaldehyde and 5 ml of tetrahydrofuran was added slowly to it under ice cooling, and stirred at room temperature for 1 hour. Water was added to the obtained mixture. The organic solvent was distilled off under reduced pressure, and extracted with ethyl acetate. The oil layer was separated, washed with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was

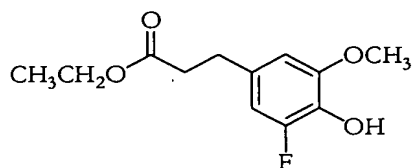
washed by hexane to obtain 3.6 g of ethyl 3-(4-benzyloxy-3-fluoro-5-methoxyphenyl)acrylate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.54 (1H, d, J=16 Hz), 7.44-7.46  
 5 (2H, m), 7.29-7.40 (3H, m), 6.89 (1H, dd, J=11 Hz, 1.9 Hz), 6.83  
 (1H, br.s), 6.32 (1H, d, J=16 Hz), 5.14 (2H, s), 4.26 (2H, q,  
 J=7.2 Hz), 3.88 (3H, s), 1.33 (3H, t, J=7.2 Hz)

Reference Example 24

3.6 g of ethyl  
 10 3-(4-benzyloxy-3-fluoro-5-methoxyphenyl)acrylate, 0.1 g of 5 %  
 palladium charcoal about 0.01 g of 36 % hydrochloric acid, 50  
 ml of ethanol were stirred under hydrogen atmosphere. After  
 stopping absorption of hydrogen gas, it was filtered, and the  
 filtrate was concentrated under reduced pressure to obtain 2.2  
 15 g of ethyl 3-(3-fluoro-4-hydroxy-5-methoxyphenyl)proionate.



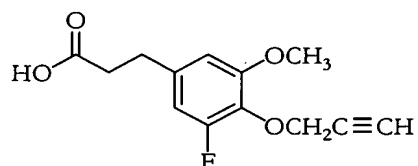
<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 6.58 (1H, dd, J=11 Hz, 2.0 Hz),  
 6.51-6.52 (1H, m), 4.13 (2H, q, J=7.1 Hz), 3.89 (3H, s), 2.86  
 (2H, t, J=7.7 Hz), 2.58 (2H, t, J=7.7 Hz), 1.24 (3H, t, J=7.1  
 20 Hz)

Reference Example 25

2.3 g of ethyl  
 3-(3-fluoro-4-hydroxy-5-methoxyphenyl)proionate, 0.63 ml of  
 propargyl bromide, 1.23 g of potassium carbonate and 300 ml of



acetonitrile were mixed and stirred under the condition of reflux for 1 hour. Then the reaction mixture was cooled to room temperature, and added ethyl acetate and filtered. The filtrate was concentrated under reduced pressure. The obtained residue, 0.54 g of lithium hydroxide, 40 ml of tetrahydrofuran and 20 ml of water were mixed, and stirred under the condition of reflux for 3 hours. Then water was added to the reaction mixture and concentrated under reduced pressure. The mixture was washed with methyl-tert-butylether, and aqueous layer was separated. 5 % hydrochloric acid was added to it, and extracted with chloroform for three times. The organic layer was dried by magnesium sulfate and concentrated under reduced pressure. The residue was washed by hexane to obtain 1.5 g of 3-{3-fluoro-5-methoxy-4-(2-propynyloxy)phenyl}proionic acid.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.59 (1H, dd,  $J=11$  Hz, 2.2 Hz), 6.55-6.56 (1H, m), 4.73 (2H, d,  $J=2.4$  Hz), 3.56 (3H, s), 2.90 (2H, t,  $J=7.7$  Hz), 2.67 (2H, t,  $J=7.7$  Hz), 2.27 (1H, t,  $J=7.1$  Hz)

#### Reference Example 26

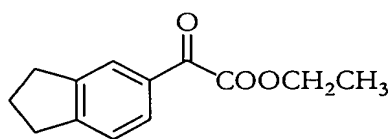
Tetrahydrofuran solution of 15.3 g of 2-naphthonitrile was dropped slowly to the mixture of 7.58 g of lithium aluminum hydride and 100 ml of tetrahydrofuran, and it was stirred at room temperature for 3 hours. Then the reaction mixture was cooled to 0 to 5  $^{\circ}\text{C}$ , and aqueous caustic soda was dropped slowly to it. After dropping, the mixture was filtered and filtrate

was concentrated under reduced pressure. Ethyl acetate and water were added to the residue, and separated into two layer. The organic layer was dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to  
 5 obtain 12.5 g of C-naphthalene-2-yl-methylamine.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.80-7.83 (3H, m), 7.74 (1H, s), 7.41-7.49 (3H, m), 4.03 (2H, s), 1.62 (2H, br.s)

#### Reference Example 27

The mixture of 31 g of aluminum chloride and 150 ml of  
 10 methylene chloride was ice cooled, 30 g of ethyl oxalyl chloride was mixed to it, and stirred under ice cooling for 30 minutes. The obtained mixture was added slowly to the mixture of 22 g of indan and 200 ml of methylene chloride under ice cooling, and stirred at room temperature for 1 hour. The reaction mixture  
 15 was mixed slowly to ice water, then organic layer was separated. The organic layer was washed with water, dried by magnesium sulfate, and concentrated under reduced pressure to obtain 37 g of crude product of ethyl indan-5-yl-oxo-acetate.

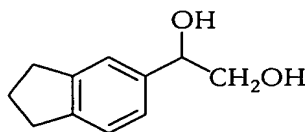


20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.84 (1H, s), 7.78 (1H, d,  $J=7.8$  Hz), 7.34 (1H, d,  $J=7.8$  Hz), 4.44 (2H, q,  $J=7.1$  Hz), 2.95-2.99 (4H, m), 2.09-2.17 (2H, m), 1.42 (3H, t,  $J=7.1$  Hz)

#### Reference Example 28

The mixture of 25 g of crude product of ethyl  
 25 indan-5-yl-oxo-acetate, 7.0 g of sodium borohydride and 250 ml of ethanol was stirred at room temperature for 1 hour and at

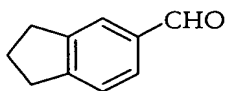
60 °C for 2 hours. Water was added to the reaction mixture, and the organic solvent was distilled off, adjusted to PH=2 by 36 % hydrochloric acid, then extracted with chloroform. The organic layer was washed with water, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was washed by hexane to obtain 11 g of indan-5-yl-ethan-1,2diol.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.22 (1H, s), 7.20 (1H, d, J=7.7 Hz), 7.11 (1H, d, J=7.7 Hz), 4.78 (1H, dd, J=8.2 Hz, 3.6 Hz), 3.62-3.75 (2H, m), 2.87-2.91 (4H, m), 2.5 (1H, br.s), 2.3 (1H, br.s), 2.03-2.10 (2H, m)

#### Reference Example 29

The mixture of 11 g of crude product of indan-5-yl-ethan-1,2-diol, 18 g of periodic acid, 100 ml of water and 100 ml of ethanol was stirred at room temperature for 12 hours. Water was added to the reaction mixture, and extracted with ethyl acetate. It was washed with water twice, then the organic solvent was distilled off. The residue was purified by silica gel column to obtain 8.1 g of indan-5-carbaldehyde.

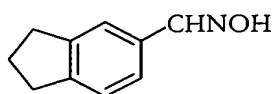


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 9.95 (1H, s), 7.73 (1H, s), 7.65 (1H, dd, J=7.7 Hz, 1.2 Hz), 7.36 (1H, d, J=7.7 Hz), 2.97 (4H, t, J=7.5 Hz), 2.08-2.17 (2H, m)

#### Reference Example 30

The mixture of 8.1 g of indan-5-carbaldehyde, 4.3 g of

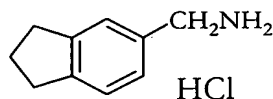
hydroxylamine hydrochloride, 5.0 g of sodium acetate, 25 ml of water and 100 ml of ethanol was stirred at room temperature for 1 hour. Water was added to the reaction mixture, and extracted with methyl=tert-butylether. It was washed with water and saturated aqueous solution of sodium sulfate, then the organic solvent was distilled off under reduced pressure. The obtained residue was washed by hexane to obtain 6.3 g of indan-5-carbaldehydeoxime.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.11 (1H, s), 7.45 (1H, s), 7.30-7.35 (2H, m), 7.22 (1H, d, J=7.7 Hz), 2.91 (4H, t, J=7.5 Hz), 2.05-2.13 (2H, m)

#### Reference Example 31

3.0 g of indan-5-carbaldehydeoxime, 0.8 g of 10 % palladium charcoal about 3.8 ml of 36 % hydrochloric acid, 90 ml of ethanol were stirred under hydrogen atmosphere. After stopping absorption of hydrogen gas, it was filtered, and the filtrate was concentrated under reduced pressure to obtain 3.2 g of indan-5-yl-methylamine hydrochloride.

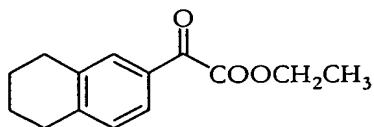


<sup>1</sup>H-NMR (CD<sub>3</sub>SOCD<sub>3</sub>, TMS) δ (ppm): 8.37 (3H, br.s), 7.34 (1H, s), 7.21-7.34 (2H, m), 3.94 (2H, s), 2.85 (4H, t, J=7.5 Hz), 1.98-2.05 (2H, m)

#### Reference Example 32

In the same way as in the Reference Example 27, 55 g of crude product of ethyl

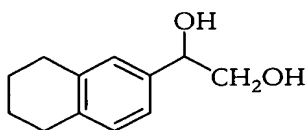
5,6,7,8-tetrahydro-naphthalene-2-yl-oxo-acetate was obtained from 58 g of Tetralin.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.69-7.72 (2H, m), 7.17 (1H, d, J=7.8 Hz), 4.44 (2H, q, J=7.2 Hz), 2.75-2.83 (4H, m), 1.17-1.85 (4H, m), 1.42 (3H, t, J=7.2 Hz)

Reference Example 33

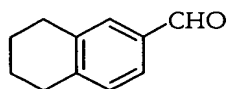
In the same way as in the Reference Example 28, 17 g of 5,6,7,8-tetrahydro-naphthalene-2-yl-ethane-1,2diol was obtained from 30 g of crude product of ethyl 5,6,7,8-tetrahydro-naphthalene-2-yl-oxo-acetate.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.01-7.04 (3H, m), 4.76 (1H, dd, J=8.1 Hz, 3.7), 3.63-3.77 (2H, m), 2.75-2.76 (4H, m), 2.4 (1H, br.s), 2.0 (1H, br.s), 1.17-1.18 (4H, m)

Reference Example 34

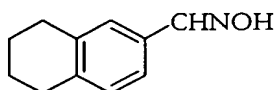
In the same way as in the Reference Example 29, 13 g of 5,6,7,8-tetrahydro-naphthalene-2-carbaldehyde was obtained from 16 g of 5,6,7,8-tetrahydro-naphthalene-2-yl-ethane-1,2diol.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 9.92 (1H, s), 7.57-7.59 (2H, m), 7.20 (1H, d, J=7.5 Hz), 2.82-2.85 (4H, m), 1.81-1.84 (4H, m)

## Reference Example 35

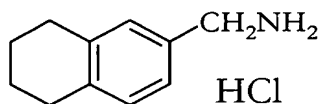
In the same way as in the Reference Example 30, 1.5 g of 5,6,7,8-tetrahydro-naphthalene-2-carbardehydroxime was obtained from 2.6 g of 5,6,7,8-tetrahydro-naphthalene-2-carbardehyde.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.08 (1H, s), 7.33 (1H, s), 7.26-7.31 (2H, m), 7.07 (1H, d,  $J=7.6$  Hz), 2.75-2.79 (4H, m), 1.78-1.82 (4H, m)

## 10 Reference Example 36

In the same way as in the Reference Example 31, 1.5 g of 5,6,7,8-tetrahydro-naphthalene-2-yl-methylamine hydrochloride was obtained from 2.6 g of 5,6,7,8-tetrahydro-naphthalene-2-carbardehydroxime.



15

$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.43 (3H, br.s), 7.17-7.19 (2H, m), 7.06-7.07 (1H, m), 3.89 (12H, d,  $J=5.1$  Hz), 2.70 (4H, s), 1.72-1.73 (4H, m)

## Reference Example 37

20 In the same way as in the Reference Example 30, 4.69 g of mixture of isomer of 4-methoxy-3-methylbenzaldehydeoxime was obtained from 5.40 g of 4-methoxy-3-methylbenzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.06 (1H, s), 7.81 (1H, br.s), 7.39 (1H, d,  $J=1.0$  Hz), 7.34 (1H, dd,  $J=8.4$  Hz, 2.0 Hz), 6.81 (1H, d,  $J=8.4$  Hz), 3.84 (3H, s), 2.22 (3H, s)

25

## Reference Example 38

In the same way as in the Reference Example 31, 4.50 g of 4-methoxy-3-methyl-benzylamine hydrochloride was obtained from 4.69 g of mixture of isomer of 4-methoxy-3-methylbenzaldehydeoxime.

5  $^1\text{H-NMR}$  (DMSO- $d_6$ , TMS)  $\delta$  (ppm): 8.26 (3H, br.s), 7.23-7.28 (2H, m), 6.94 (1H, d,  $J=8.2$  Hz), 3.88 (2H, s), 3.77 (3H, s), 2.13 (3H, s)

Reference Example 39

10 In the same way as in the Reference Example 30, 5.00 g of mixture of isomer of 4-phenoxy-benzaldehydeoxime was obtained from 4.96 g of 4-phenoxy-benzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.11 (1H, s), 7.54 (2H, d,  $J=8.7$  Hz), 7.32-7.40 (3H, m), 7.15 (1H, t,  $J=7.4$  Hz), 7.04 (2H, d,  $J=7.7$  Hz), 6.99 (2H, d,  $J=8.7$  Hz)

15 Reference Example 40

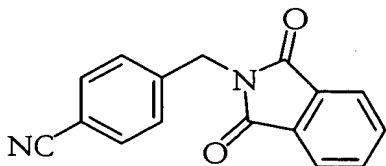
In the same way as in the Reference Example 31, 4.71 g of 4-phenoxy-benzylamine hydrochloride was obtained from 4.61 g of mixture of isomer of mixture of isomer of 4-phenoxy-benzaldehydeoxime.

20  $^1\text{H-NMR}$  (DMSO- $d_6$ , TMS)  $\delta$  (ppm): 8.32 (3H, br.s), 7.48 (2H, d,  $J=8.7$  Hz), 7.36-7.43 (2H, m), 7.15 (1H, t,  $J=7.4$  Hz), 6.95-7.04 (4H, m), 3.97 (2H, s)

Reference Example 41

25 9.5 g of potassium phthalimide, 10 g of 4-cyanobenzylbromide, 100 ml of dimethylformi were mixed, and stirred at 100 °C for 4 hours. Then the reaction mixture was cooled to room temperature, then water was added to it, and extracted with ethyl acetate. The oil layer was washed

successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 13 g of N-(4-cyano-benzyl)phthalimide.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.87 (2H, dd,  $J=5.4$  Hz, 2.9 Hz), 7.74 (2H, dd,  $J=5.4$  Hz, 2.9 Hz), 7.62 (2H, d,  $J=8.3$  Hz), 7.52 (2H, d,  $J=8.3$  Hz), 4.89 (2H, s)

#### 10 Reference Example 42

0.90 g of hydrazine hydrate was dropped to mixture of 4.00 g of N-(4-cyano-benzyl)phthalimide and 15 ml of methanol, and stirred at 65 °C for 2 hours and half. Then the reaction mixture was cooled to room temperature, then water was added to it, and concentrated under reduced pressure. 1N hydrochloric acid was added to the residue, and it was filtered. Ethyl acetate was added to the filtrate, and it was washed successively with 25 % aqueous solution of caustic soda, saturated aqueous solution of sodium sulfate, dried by magnesium sulfate, and concentrated under reduced pressure to obtain 0.84 g of crude 4-cyanobenzylamine.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.61 (2H, d,  $J=8.2$  Hz), 7.44 (2H, d,  $J=7.9$  Hz), 3.95 (2H, s), 1.55 (2H, br.s)

#### Reference Example 43

25 In the same way as in the Reference Example 30, 6.4 g of mixture of isomer of 4-banzylxy-benzaldehydeoxime was obtained



from 6.39 g of 4-benzyloxy-benzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.08 (1H, s), 7.50 (2H, d,  $J=8.8$  Hz), 7.30-7.47 (5H, m), 6.98 (2H, d,  $J=8.7$  Hz), 5.09 (2H, s)

Reference Example 44

5            In the same way as in the Reference Example 31, 4.0 g of 4-hydroxy-benzylamine hydrochloride was obtained from 6.4 g of mixture of isomer of mixture of isomer of 4-benzyloxy-benzaldehydeoxime.

10            $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ , TMS)  $\delta$  (ppm): 9.68 (1H, br.s), 8.31 (3H, br.s), 7.28 (2H, d,  $J=7.6$ Hz) 6.79 (2H, d,  $J=7.6$ Hz), 3.84-3.88 (2H, m)

Reference Example 45

15            1.87 g of 2,6-dimethylnaphthalene and 200 ml of 50 % aqueous acetic acid were mixed, and suspended at  $80^\circ\text{C}$ . The mixed solution of 26.3 g of ammonium cerium(IV) nitrate and 400 ml of 50 % aqueous acetic acid was dropped to the said suspension over period for about 1 hour. Further it was stirred at  $80^\circ\text{C}$  for 1 hour. Then the reaction solution was cooled to room temperature, and extracted with chloroform. The organic layer was washed successively with water, saturated aqueous solution of sodium bicarbonate, saturated aqueous solution of sodium chloride, concentrated under reduced pressure. The residue was purified by silica gel column to obtain 0.90 g of 6-methyl-2-naphthoaldehyde.

20            $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 10.1 (1H, s), 8.29 (1H, s), 7.80-7.95 (3H, m), 7.68 (1H, s), 7.42 (1H, dd,  $J=8.4$  Hz, 1.6 Hz), 2.56 (3H, s)

Reference Example 46

In the same way as in the Reference Example 30, 1.56 g

of mixture of isomer of 6-methyl-2-naphtoaldehydeoxime was obtained from 1.74 g of 6-methyl-2-naphtoaldehyde.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.27 (1H, s), 7.83 (1H, s), 7.71-7, 81 (3H, m), 7.60 (1H, s), 7.41 (1H, s), 7.34 (1H, dd, J=8.5 Hz, 1.7 Hz), 2.51 (3H, s)

#### Reference Example 47

In the same way as in the Reference Example 31, 1.60 g of C-(6-methyl-naphthlene-2-yl)-methylaniline hydrochloride was obtained from 1.46 g of mixture of isomer of 6-methyl-2-naphtoaldehydeoxime.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, TMS) δ (ppm): 8.64 (3H, br.s), 7.96 (1H, s), 7.86 (1H, d, J=8.7 Hz), 7.80 (1H, d, J=8.3 Hz), 7.71 (1H, s), 7.60-7.64 (1H, m), 7.37-7.43 (1H, m), 4.10-4.20 (2H, m), 2.48 (3H, s)

#### Reference Example 48

In the same way as in the Reference Example 45, 0.85 g of 7-methyl-2-napthoaldehyde was obtained from 1.87 g of 2,7-dimethylnaphthalene.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 10.1 (1H, s), 8.25 (1H, s), 7.89 (2H, d, J=0.8 Hz), 7.81 (1H, d, J=8.3 Hz), 7.77 (1H, s), 7.48 (1H, dd, J=8.7 Hz, 1.5 Hz), 2.55 (3H, s)

#### Reference Example 49

In the same way as in the Reference Example 30, 0.78 g of mixture of isomer of 7-methyl-2-naphtoaldehydeoxime was obtained from 1.32 g of 7-methyl-2-naphtoaldehyde.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.27 (1H, s), 7.70-7, 82 (4H, m), 7.61 (1H, s), 7.50 (1H, br.s), 7.34 (1H, dd, J=8.3 Hz, 1.7 Hz), 2.51 (3H, s)

## Reference Example 50

In the same way as in the Reference Example 31, 0.72 g of C-(7-methyl-naphthlene-2-yl)-methylamine hydrochloride was obtained from 0.78 g of mixture of isomer of 7-methyl-2-naphtoaldehydeoxime.

$^1\text{H-NMR}$  (DMSO- $d_6$ , TMS)  $\delta$  (ppm): 8.54 (3H, br.s), 7.89-7.93 (2H, m), 7.84 (1H, d,  $J=8.3$  Hz), 7.66 (1H, s), 7.56 (1H, dd,  $J=8.5$  Hz, 1.6 Hz), 7.39 (1H, dd,  $J=8.5$  Hz, 1.6 Hz), 4.16 (2H, s), 2.48 (3H, s)

## 10 Reference Example 51

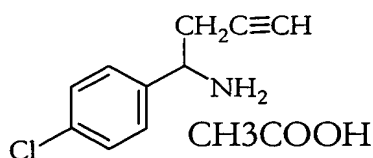
500 ml of tetrahydrofuran and 8.7 g of potassium hydride (mixture with liquid paraffin, content 35 %) were mixed. It was cooled to  $0^\circ\text{C}$ , and mixed with 15 g of ethyl 4-chlorophenylacetate, then stirred at  $0^\circ\text{C}$  for 30 minutes. 5.7 ml of 3-bromopropyn was mixed with it, and mixed at  $0^\circ\text{C}$  for 30 minutes and at room temperature for 8 hours. Water was added to the reaction mixture, and extracted with ethyl acetate. The oil layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column to obtain 13 g of ethyl 2-(4-chlorophenyl)-4-pentynic acid. 13 g of ethyl 2-(4-chlorophenyl)-4-pentynic acid, 27 ml of 20 % aqueous solution of caustic soda and about 60 ml of ethanol were mixed at  $0^\circ\text{C}$ , and stirred at  $70^\circ\text{C}$  for 1 hour. Water was added to the reaction mixture, then adjusted to  $\text{PH}=2$  by 5 % hydrochloric acid, and extracted with ethyl acetate. The oil layer was washed

successively with buffer solution of PH6.8, saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 10 g of 2-(4-chlorophenyl)-4-pentynic acid.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.20-7.35 (4H, m), 3.80 (1H, t,  $J=7.6$  Hz), 2.90 (1H, ddd,  $J=17$  Hz, 7.6 Hz, 2.7 Hz), 2.64 (1H, ddd,  $J=17$  Hz, 7.6 Hz, 2.7 Hz), 1.97 (1H, t,  $J=2.7$  Hz)

Reference Example 52

- 1.0 g of 2-(4-chlorophenyl)-4-pentynic acid, 1.2 ml of diphenylphosphoryl azide, 1 ml of triethylamine and 15 ml of tert-butanol were mixed, stirred under the condition of reflux for 3 hours. The reaction mixture was cooled, then water was added to it, and extracted with ethyl acetate. The oil layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate, saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue (tert-butyl {1-(4-chlorophenyl)-3-butynylamine} carbamate), 1 ml of trifluoroacetic acid, 6 ml of acetic acid and 3 ml of water was mixed, and stirred at 70 °C for 3 hours. The reaction mixture was concentrated under reduced pressure to obtain 0.85 g of crude product of 1-(4-chlorophenyl)-3-butynylamine acetic acid salt. The obtained 1-(4-chlorophenyl)-3-butynylamine acetic acid salt was used as it is without purification.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.20-7.41 (4H, m), 4.8 (1H, br.s), 3.02-3.18 (1H, m), 2.62-2.76 (2H, m), 2.02 (1H, t,  $J=2.7$  Hz), 1.43 (9H, s)

#### Reference Example 53

5            10 g of 4-chloroacetophenone, 12 g of formamide and 1.0 g of formic acid were mixed, and stirred at 170 °C for 6 hours. The reaction mixture was cooled to room temperature, then water was added to it, and extracted with ethyl acetate. The oil layer was washed successively with water, and concentrated under  
10 reduced pressure. The obtained residue and 36 % hydrochloric acid were mixed, and stirred at 100 °C for 1 hour. Water was added to the reaction mixture, and it was washed by methyl-tert-butylether. The aqueous layer was adjusted to PH=10 by 20 % aqueous solution of caustic soda, then extracted with  
15 methyl-tert-butylether twice. The oil layer was washed successively with water and saturated aqueous solution of sodium chloride, dried by potassium carbonate, concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 8.4 g of 1-(4-chlorophenyl)-ethylamine.

20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.27-7.30 (4H, m), 4.10 (1H, q,  $J=6.5$  Hz), 1.56 (2H, br.s), 1.36 (3H, d,  $J=6.5$  Hz)

#### Reference Example 54

In the same way as in the Reference Example 53, 6.6 g of 1-(3,4-dichlorophenyl)ethylamine was obtained from 9.5 g of  
25 3,4-dichloroacetophenone.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.46 (1H, d,  $J=2.2$  Hz), 7.38 (1H, d,  $J=8.2$  Hz), 7.18 (1H, dd,  $J=8.2$  Hz, 2.2 Hz), 4.19 (1H, q,  $J=6.5$  Hz), 1.53 (2H, br.s), 1.35 (3H, d,  $J=6.5$  Hz)

## Reference Example 55

In the same way as in the Reference Example 53, 5.3 g of 1-naphthalene-2-ylethylamine was obtained from 4.1 g of 2-acetylnaphthalene.

5  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.76-7.84 (4H, m), 7.41-7.54 (3H, m), 4.28 (1H, q,  $J=6.6$  Hz), 1.59 (2H, br.s), 1.46 (3H, d,  $J=6.5$  Hz)

## Reference Example 56

3.0 g of 2-acetyl-5,6,7,8-tetrahydro-naphthalene, 3.1 g  
 10 of formamide and 0.34 g of formic acid were mixed, and stirred at 170 °C for 6 hours. The reaction mixture was cooled to room temperature, then water was added to it, and extracted with ethyl acetate. The oil layer was washed successively with water, concentrated under reduced pressure. The obtained residue and  
 15 36 % hydrochloric acid were mixed, and stirred at 100 °C for 1 hour. Water was added to the reaction mixture, and the product was filtered off. The product was dried under reduced pressure to obtain 2.5 g of  
 1-(5,6,7,8-tetrahydronaphthalene-2yl)-ethylamine  
 20 hydrochloride.

$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.51 (3H, br.s), 7.19-7.22 (2H, m), 7.08 (1H, d,  $J=8.0$  Hz), 4.23-4.29 (1H, m), 2.70-2.71 (4H, m), 1.72-1.74 (4H, m), 1.48 (3H, d,  $J=6.8$  Hz)

## Reference Example 57

25 4.75 g of 4-chloro-2-fluorobenzaldehyde and 30 ml of methanol were mixed. It was cooled to 0 °C, and 0.57 g of sodium borohydride was added to it, and stirred at 0 °C for 30 minutes and at room temperature for 1 hour. Water was added to the reaction

mixture, and concentrated under reduced pressure. The obtained residue was extracted with chloroform. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure to obtain 4.57 g of (4-chloro-2-fluorophenyl)methanol.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.37 (1H, t,  $J=8.0$  Hz), 7.12-7.17 (1H, m), 7.08 (1H, dd,  $J=9.7$  Hz, 1.9 Hz), 4.73 (2H, s), 2.04 (1H, br.s)

10 Reference Example 58

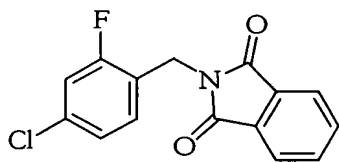
4.75 g of (4-chloro-2-fluoro-phenyl)methanol, 4.31 g of triethylamine and 60 ml of tetrahydrofuran were mixed. It was cooled to  $0^\circ\text{C}$ , then 4.24 g of methanesulfonyl chloride was added to it, and stirred at  $0^\circ\text{C}$  for 30 minutes, at room temperature for 2 hours. Water was added to the reaction mixture, and concentrated under reduced pressure. The obtained residue was extracted with chloroform. The organic layer was washed successively with 5 % hydrochloric acid, saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure to obtain (4-chloro-2-fluorobenzyl) methanesulfonate.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.37-7.43 (1H, m), 7.14-7.22 (2H, m), 5.25 (2H, s), 3.01 (3H, s)

Reference Example 59

25 2.64 g of potassium phthalimide, 3.4 g of (4-chloro-2-fluoro-benzyl) methanesulfonate and 80 ml of N,N-dimethylformamide were mixed, and stirred at room temperature for 2 hours. Then water was added to the reaction mixture, and

extracted with chloroform. The organic layer was washed successively with 5 % hydrochloric acid, water, saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 2.92 g of N-(4-chloro-2-fluoro-benzyl)phthalimide.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.85-7.88 (2H, m), 7.71-7.75 (2H, m), 7.27-7.33 (1H, m), 7.05-7.11 (2H, m), 4.89 (2H, s)

#### 10 Reference Example 60

0.90 g of hydrazine hydrate was dropped to the mixed solution of 2.7 g of N-(4-chloro-2-fluoro-benzyl)phthalimide and 50 ml of methanol, and stirred at 65 °C for 2 hours and half. Then the reaction mixture was cooled to room temperature, water was added to it, and concentrated under reduced pressure. 1N-hydrochloric acid was added to the residue, and filtered. Chloroform was added to the filtrate, then 25 % aqueous solution of sodium hydroxide was added to it until the aqueous layer of the mixed solution turned to basic, and separated to two layer. The obtained organic layer was washed successively with saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. 20 ml of acetonitrile and 2 ml of concentrated hydrochloric acid were added to the obtained residue. Then the residue which it was concentrated under reduced pressure was washed by hexane to obtain 1.13 g of 4-chloro-2-fluoro-benzylamine hydrochloride.



$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.36 (3H, br.s), 7.51-7.68 (2H, m), 7.40 (1H, d,  $J=8.4$  Hz), 4.04 (2H, s)

Reference Example 61

In the same way as in the Reference Example 57, 3.98 g of (4-chloro-3-fluoro-phenyl)methanol was obtained from 3.96 g of .

4-chloro-3-fluorobenzaldehyde.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.33-7.39 (1H, m), 7.15-7.20 (1H, m), 7.05-7.09 (1H, m), 4.67 (2H, s), 1.83 (1H, br.s)

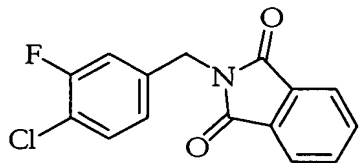
Reference Example 62

In the same way as in the Reference Example 58, 5.77 g of (4-chloro-3-fluoro-benzyl) methanesulfonate was obtained from 3.98 g of (4-chloro-3-fluoro-phenyl)methanol.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.42-7.46 (1H, m), 7.20-7.24 (1H, m), 7.12-7.17 (1H, m), 5.19 (2H, s), 3.00 (3H, s)

Reference Example 63

In the same way as in the Reference Example 59, 6.23 g of N-(4-chloro-3-fluoro-benzyl)phthalimide was obtained from 5.77 g of (4-chloro-3-fluoro-benzyl) methanesulfonate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.84-7.88 (2H, m), 7.71-7.75 (2H, m), 7.30-7.36 (1H, m), 7.22 (1H, dd,  $J=9.5$  Hz, 1.9 Hz), 7.14-7.18 (1H, m), 4.80 (2H, s)

Reference Example 64

In the same way as in the Reference Example 60, 1.2 g of 4-chloro-3-fluoro-benzylamine hydrochloride was obtained from

6.23 g of N-(4-chloro-3-fluoro-benzyl)phthalimide.

$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.35 (3H, br.s), 7.56-7.70 (2H, m), 7.33-7.49 (1H, m), 4.05 (2H, s)

Reference Example 65

5           In the same way as in the Reference Example 45, 0.25 g of 6-fluoro-2-naphthoaldehyde was obtained from 1.0 g of 2-fluoro-6-methylnaphthalene.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 10.1 (1H, s), 8.33 (1H, s), 7.95-8.05 (2H, m), 7.88 (1H, d,  $J=8.4$  Hz), 7.52 (1H, dd,  $J=9.4$  Hz, 2.4 Hz), 7.37 (1H, dt,  $J=8.6$  Hz, 2.4 Hz)

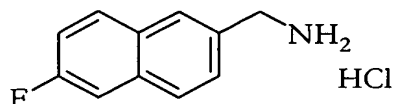
Reference Example 66

          In the same way as in the Reference Example 30, 0.53 g of mixture of isomer of 6-fluoro-2-naphthoaldehydeoxime was obtained from 0.55 g of 6-fluoro-2-naphthoaldehyde.

15        $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 8.26 (1H, s), 7.75-7.90 (4H, m), 7.42-7.47 (2H, m), 7.28 (1H, dt,  $J=8.8$  Hz, 2.6 Hz)

Reference Example 67

          In the same way as in the Reference Example 31, 0.51 g of C-(6-fluoro-naphthalene-2-yl)-methylanilinehydrochloride was obtained from 0.53 g of mixture of isomer of 6-fluoro-2-naphthoaldehydeoxime.

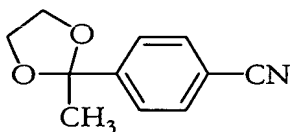


$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.57 (3H, br.s), 7.94-8.10 (3H, m), 7.66-7.78 (2H, m), 7.48 (1H, dt,  $J=8.8$  Hz, 2.2 Hz), 4.17 (2H, s)

Reference Example 68

10 g of 4-cyanoacetophenone, 6.4 g of ethylene glycol,

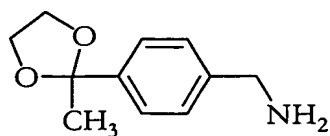
about 0.1 g of p-toluenesulfonic acid and 150 ml of toluene were stirred under the condition of reflux with dehydration for 3 hours. Then 5 ml of ethylene glycol was mixed again, and stirred under the condition of reflux with dehydration for 3 hours. The reaction mixture was cooled to room temperature, then washed successively with water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The obtained residue was washed by hexane to obtain 11 g of 4-(2-methyl-[1,3]dioxolane-2-yl)benzonitrile.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.58-7.65 (4H, m), 4.02-4.15 (2H, m), 3.71-3.86 (2H, m), 1.63 (3H, s)

#### Reference Example 69

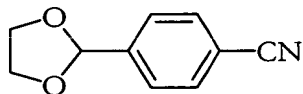
4.4 g of lithium aluminium hydride was mixed with 150 ml of tetrahydrofuran, the mixture of 10 g of 4-(2-methyl-[1,3]dioxolane-2-yl)benzonitrile and 30 ml of tetrahydrofuran was slowly mixed with it. The mixture was stirred under the condition of reflux for 2 hours. It was cooled to room temperature, and mixed slowly with 9 ml of 20 % aqueous solution of sodium hydroxide and 11 ml of water, then stirred at room temperature for 1 hour. Then it was filtered to remove a solid. The obtained solution was concentrated under reduced pressure to obtain 11 g of 4-(2-methyl-[1,3]dioxolane-2-yl)benzylamine.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.44 (2H, d,  $J=8.1$  Hz), 7.28 (2H, d,  $J=8.1$  Hz), 4.02-4.05 (2H, m), 3.86 (2H, s), 3.76-3.79 (2H, m), 1.65 (3H, s) 1.46 (2H, br.s)

#### 5 Reference Example 70

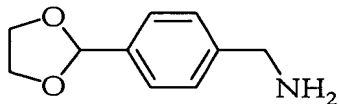
In the same way as in the Reference Example 68, 13 g of 4-([1,3]dioxolane-2-yl)benzonitrile was obtained by using 11 g of 4-cyanobenzaldehyde, 8.6 g of ethylene glycol.



10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.67 (2H, d,  $J=8.4$  Hz), 7.59 (2H, d,  $J=8.4$  Hz), 5.85 (1H, s), 4.09-4.11 (2H, m), 4.05-4.07 (2H, m)

#### Reference Example 71

15 In the same way as in the Reference Example 69, 13 g of 4-([1,3]dioxolane-2-yl)benzylamine was obtained by using 5.5 g of lithium aluminum hydride and 13 g of 4-([1,3]dioxolane-2-yl)benzonitrile.

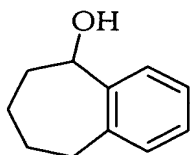


20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.44 (2H, d,  $J=8.0$  Hz), 7.32 (2H, d,  $J=8.0$  Hz), 5.80 (1H, s), 4.07-4.16 (2H, m), 4.01-4.05 (2H, m), 3.88 (2H, s) 1.43 (2H, br.s)

#### Reference Example 72

25 g of 1-benzosuberone, 300 ml of ethanol and 3.0 g of sodium borohydride were mixed at room temperature for 3 hours.

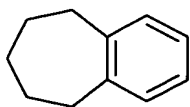
Saturated aqueous solution of ammonium chloride was added to the mixture, and concentrated under reduced pressure. Ethyl acetate was added to the residue, and extracted. The organic layer was washed with water and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure to obtain 25 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-5-ol.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.43 (1H, d,  $J=7.1$  Hz), 7.01-7.22 (3H, m), 4.93 (1H, d,  $J=5.5$  Hz), 2.91 (1H, dd,  $J=14$  Hz, 8.3 Hz), 2.71 (1H, ddd,  $J=14$  Hz, 11 Hz, 1.7 Hz), 2.02-2.07 (1H, m), 1.93-1.97 (1H, m), 1.75-1.86 (4H, m), 1.50-1.51 (1H, m)

#### Reference Example 73

25 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-5-ol, 2.4 g of 10 % palladium charcoal, 200 ml of ethanol and 0.5 ml of 36 % hydrochloric acid were mixed under hydrogen current until the stopping of absorption of hydrogen gas. It was filtered, and filtrate was concentrated under reduced pressure. Hexane was added to the residue, and washed with water, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure to obtain 22 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene.

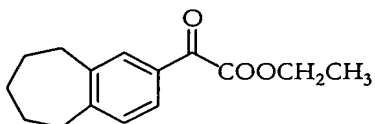


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.08 (4H, s), 2.77-2.80 (4H, m),

1.80-1.86 (2H, m), 1.63-1.69 (4H, m)

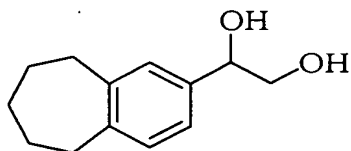
Reference Example 74

In the same way as in the Reference Example 27, 12 g of crude product of ethyl 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl-oxo-acetate was obtained by using 7.2 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene, 6.2 g of ethyl oxalyl chloride and 6.3 g of aluminum chloride.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.70-7.73 (1H, m), 7.21 (1H, d, J=4.6 Hz), 7.09 (1H, s), 4.44 (2H, q, J=7.0 Hz), 2.77-2.87 (4H, m), 1.80-1.88 (2H, m), 1.63-1.67 (4H, m), 1.42 (3H, t, J=7.0 Hz)  
Reference Example 75

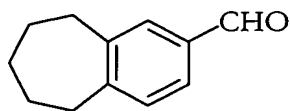
In the same way as in the Reference Example 28, 5.1 g of crude product of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl-ethane-1,2diol was obtained by using 7.3 g of ethyl 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl-oxo-acetate, 2.2 g of sodium borohydride.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.07-7.10 (3H, m), 4.76 (1H, dd, J=7.9 Hz, 3.6 Hz), 3.68-3.77 (2H, m), 2.76-2.80 (4H, m), 2.38 (1H, br.s), 2.02 (1H, br.s), 1.65-1.86 (2H, m), 1.63-1.64 (4H, m)

## Reference Example 76

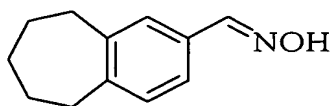
In the same way as in the Reference Example 29, 5.1 g of crude product of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carbaldehyde was obtained by using 5.0 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl-ethane-1,2diol, 2.2 g of sodium periodic acid.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 9.93 (1H, s), 7.58-7.60 (2H, m), 7.24-7.25 (1H, m), 2.85-2.89 (4H, m), 1.83-1.89 (2H, m), 1.65-1.69 (4H, m)

## Reference Example 77

In the same way as in the Reference Example 30, 1.3 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carbaldehydeoxime was obtained by using 1.0 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carbaldehyde, 0.52 g of hydroxylamine hydrochloride.

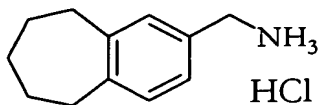


<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 8.08 (1H, s), 7.27-7.33 (1H, m), 7.07-7.15 (2H, m), 3.33 (1H, s), 2.77-2.82 (4H, m), 1.80-1.84 (2H, m), 1.60-1.70 (4H, m)

## Reference Example 78

In the same way as in the Reference Example 31, 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-methylamine hydrochloride was obtained by using 1.2 g of 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl-carbaldehydeox

ime.



$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.33 (3H, br.s), 7.12-7.22 (3H, m), 3.92 (2H, q,  $J=5.9$  Hz), 2.75-2.77 (4H, m), 1.77-1.83 (2H, m), 1.50-1.60 (4H, m)

Reference Example 79

According to Synlett, 2000, No.12, p1801 to 1803, 10 g of 4-bromobenzonitrile, trisdibenzylideneacetonepalladium(0), 0.98 g of 2-(di tert-butylphosphino)biphenyl and 200 ml of dimethylimidazoline were mixed at room temperature for 5 minutes hours. Then 16.9 ml of hexamethyldisilane and 2.0 g of water were added to it and washed with water for five times, dried by magnesium sulfate, concentrated under reduced pressure. The residue was purified by silica gel column to obtain 8.0 g of 4-trimethylsilylbenzonitrile.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.60 (4H, s), 0.29 (9H, s)

Reference Example 80

In the same way as in the Reference Example 69, 0.65 g of 4-trimethylsilylbenzylamine was obtained by using 0.66 g of 4-trimethylsilylbenzonitrile, 0.29 g of lithium aluminum hydride.

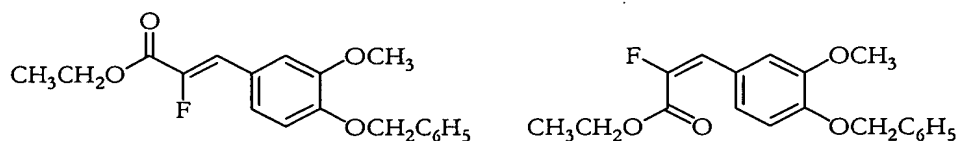
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.48-7.51 (2H, m), 7.31 (2H, d,  $J=8.0$  Hz), 3.86 (2H, s), 1.43 (2H, br.s), 0.25 (9H, s)

Reference Example 81

2.2 g of ethyl 2-fluoro-2-diethylphosphonoacetate and 50 ml of tetrahydrofuran were mixed, 0.40 g of sodium hydride (content 55 %) was added to it under ice cooling, and stirred for 10 minutes.



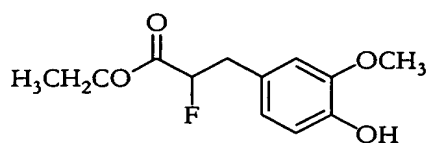
Then the mixture of 2.0 g of 4-benzyloxy-3-methoxybenzaldehyde and 5 ml of tetrahydrofuran was slowly added to it, and stirred at room temperature for 3 hours. Water was added to the obtained mixture, the organic solvent was distilled off under reduced pressure, and extracted with ethyl acetate. The oil layer was separated, then it was washed with water, 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, concentrated under reduced pressure. The obtained residue was purified by silica gel column to obtain 2.8 g of crude product of ethyl 3-(3-methoxy-4-benzyloxyphenyl)-2-fluoroacrylate (mixture of cis-form and trans-form).



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.27-7.44 (6H, m), 7.13 (0.3H, dd, J=8.6 Hz, 1.7 Hz, ), 7.01 (0.6H, dd, J=8.3 Hz, 1.9 Hz, ), 6.79-6.90 (2H, m), 5.20 (0.6H, s), 5.18 (1.4H, s), 4.25-4.36 (2H, m), 3.91 (3H, s), 1.27-1.36 (3H, m)

#### Reference Example 82

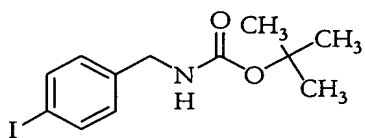
In the same way as in the Reference Example 11, 2.0 g of crude product of ethyl 3-(3-methoxy-4-hydroxyphenyl)-2-fluoropropionate was obtained by using 2.6 g of crude product of ethyl 3-(3-methoxy-4-benzyloxyphenyl)-2-fluoroacrylate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 6.85 (1H, d,  $J=8.0$  Hz), 6.70-6.75 (2H, m), 5.52 (1H, br.s), 5.04 (1H, ddd,  $J=49$  Hz, 7.6 Hz, 4.2 Hz), 4.22 (2H, q,  $J=7.1$  Hz), 3.88 (3H, s), 3.06-3.18 (2H, m),  
 5 1.27 (3H, t,  $J=7.1$  Hz)

#### Reference Example 83

1.0 g of 4-iodobenzylamine, 1.1 g of di tert butyl dicarbonete, 0.9 ml of triethylamine, about 10 ml of dimethylaminopyridine and 2 ml of tetrahydrofuran were mixed  
 10 at room temperature for 4 hours. Then water was added to it, and extracted with ethyl acetate. The oil layer was separated, washed with 5 % hydrochloric acid twice, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated  
 15 under reduced pressure to obtain 1.5 g of crude product of tert butyl (4-iodobenzyl)carbamate.

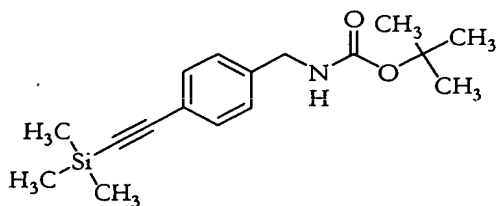


$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.64 (2H, d,  $J=8.2$  Hz), 7.03 (2H, d,  $J=8.2$  Hz), 4.83 (1H, br.s), 4.25 (2H, d,  $J=5.6$  Hz), 1.45 (9H, s)

#### 20 Reference Example 84

1.5 g of tert butyl (4-iodobenzyl)carbamate, 1.3 ml of trimethylsilyl acetylene, 97 mg of bis(triphenylphosphine)palladium(II) dichloride, 1.3 ml of

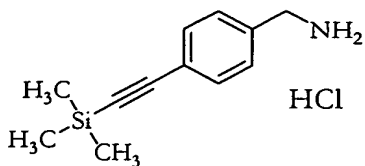
triethylamine, 26 mg of copper iodide(I) and 30 ml of dimethylformamide were mixed at 50 °C for 4 hours. Then water was added to it, and extracted with ethyl acetate. The oil layer was separated, washed with 5 % hydrochloric acid, saturated aqueous solution of sodium bicarbonate and saturated aqueous solution of sodium chloride, dried by magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to obtain 0.55 g of tert butyl {(4-trimethylsilyl)ethynyl}benzyl}carbamate.



$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , TMS)  $\delta$  (ppm): 7.42 (2H, d,  $J=8.1$  Hz), 7.20 (2H, d,  $J=8.1$  Hz), 4.82 (1H, br.s), 4.30 (2H, d,  $J=5.1$  Hz), 1.46 (9H, s), 0.24 (9H, s)

Reference Example 85

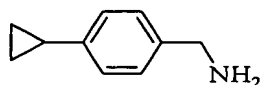
0.55 g of tert butyl {(4-trimethylsilyl)ethynyl}benzyl}carbamate, 0.42 ml of trifluoroacetic acid, 20 ml of acetic acid and 10 ml of water were mixed at 60 °C for 2 hours. Then it was concentrated under reduced pressure to obtain 0.52 g of crude product of (4-trimethylsilyl)ethynyl}benzylamine acetic acid salt.



$^1\text{H-NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , TMS)  $\delta$  (ppm): 8.15 (3H, br.s), 7.52 (2H, d,  $J=8.4$  Hz), 7.44 (2H, d,  $J=8.2$  Hz), 4.05 (2H, s), 0.23 (9H, s)

## Reference Example 86

In the same way as in the Reference Example 69, 0.51 g of 4-cyclopropylbenzylamine was obtained by using 0.58 g of 4-cyclopropylcyanobenzene which was produced according to the method described Tetrahedron Letters 43, 6987 to 6999, and 0.27g of lithium aluminum hydride.



<sup>1</sup>H-NMR (CDCl<sub>3</sub>, TMS) δ (ppm): 7.19 (2H, d, J=8.1 Hz), 7.04 (2H, d, J=8.1 Hz), 3.81 (2H, s), 1.85-1.91 (1H, m), 1.45 (2H, br.s), 0.92-0.96 (2H, m), 0.65-0.69 (2H, m)

Next formulation examples are shown. Parts represent parts by weight.

## Formulation Example 1

Fifty parts of each of the compounds of the present invention 1 to 129, 3 parts of calcium ligninsulfonate, 2 parts of magnesium laurylsulfate and 45 parts of synthetic hydrated silica are pulverized and mixed well to give wettable powders of each compound.

## Formulation Example 2

Twenty parts of each of the compounds of the present invention 1 to 129 and 1.5 parts of sorbitan trioleate are mixed with 28.5 parts of an aqueous solution containing 2 parts of polyvinyl alcohol, and wet-pulverized finely. To the obtained mixture, 40 parts of an aqueous solution containing 0.05 part of xanthan gum and 0.1 part of aluminium magnesium silicate is added and further 10 parts of propylene glycol are added to give

a flowable of each compound.

#### Formulation Example 3

Two parts of each of the compounds of the present invention 1 to 129, 88 parts of kaolin clay and 10 parts of talc are pulverized and mixed well to give a dust of each compound.

#### Formulation Example 4

Five parts of each of the compounds of the present invention 1 to 129, 14 parts of polyoxyethylenestyryl phenyl ether, 6 parts of calcium dodecylbenzenesulfonate and 75 parts of xylene are mixed well to give an emulsifiable concentrate of each compound.

#### Formulation Example 5

Two parts of each of the compounds of the present invention 1 to 129, 1 part of synthetic hydrated silica, 2 parts of calcium ligninsulfonate, 30 parts of bentonite and 65 parts of kaolin clay are pulverized and mixed well, and water is added thereto and kneaded, granulated and dried to give a granule of each compound.

#### Formulation Example 6

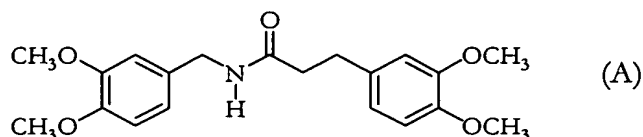
Ten parts of each of the compounds of the present invention 1 to 129, 35 parts of white carbon containing 50% by weight of ammonium polyoxyethylenealkyl ether sulfate and 55 parts of water are mixed and wet pulverized finely to give a formulation of each compound.

Next, it is shown that the compound of the present invention are useful for controlling plant diseases in test examples.

Additionally, the control effect was evaluated by visually observing the area of a lesion on a sample plant in investigation and comparing the area of a lesion on a non-treatment plant and

the area of a lesion on a treated plant with the compound of the present invention.

And the compound (A) shown by the formula described below which is described Journal of Chemical Society, Perkin Transactions I, 6, p.661 (1976) is also used for the test.



#### Test Example 1

Sand loam was compacted in a plastic pot, and a tomato (variety: Ponterosa) was seeded and grown in a green house for 20 days. Each of the compounds of the present invention 1 to 27, 29 to 35, 37 to 79, 82 to 93, 95, 96, 98 to 112, 115 to 118 and 120 to 123; and the compound (A) was formulated according to Formulation Example 6, then, diluted with water to provide prescribed concentration (500 ppm), and these diluted solutions were sprayed onto stems and leaves so as to give sufficient adhesion on the surface of the tomato leaves. After spraying, the liquid on the stem was air-dried, and a suspension of zoosporangia of *Phytophthora infestans* (about 10,000 zoosporangia were contained in 1ml of the suspension) was inoculated by spraying (the amount of the sprayed suspension was about 2 ml for one plant). After inoculation, the plant was first grown for one day at 23°C under 90 % or more humidity, then further grown for 4 days in the green house, which was 24°C in daytime and 20°C in night-time. Then, the areas of a lesion of the plants were observed.

As a result, the lesion areas on the plants treated with

the compounds of the present invention 1 to 27, 29 to 35, 37 to 79, 82 to 93, 95, 96, 98 to 112 and 115 to 118 and 120 to 123 were not more than 10% of the lesion area on a non-treatment plant. The lesion areas on the plant treated with the compound (A) was 76 to 100 % of the lesion area on a non-treatment plant.

#### Test Example 2

Sand loam was compacted in a plastic pot, and a tomato (variety: Ponterosa) was seeded and grown in a green house for 20 days. Each of the compounds of the present invention 94, 113, 119 and 125 to 129 was formulated according to Formulation Example 6, then, diluted with water to provide prescribed concentration (200 ppm), and these diluted solutions were sprayed onto stems and leaves so as to give sufficient adhesion on the surface of the tomato leaves. After spraying, the liquid on the stem was air-dried, and a suspension of zoosporangia of *Phytophthora infestans* (about 10,000 zoosporangia were contained in 1ml of the suspension) was inoculated by spraying (the amount of the sprayed suspension was about 2 ml for one plant). After inoculation, the plant was first grown for one day at 23°C under 90 % or more humidity, then further grown for 4 days in the green house, which was 24°C in daytime and 20°C in night-time. Then, the areas of a lesion of the plants were observed.

As a result, the lesion areas on the plants treated with the compounds of the present invention 94, 113, 119 and 125 to 129 were not more than 10% of the lesion area on a non-treatment plant.

#### Test Example 3

Sand loam was compacted in a plastic pot, and a grape

(variety: Berry A) was seeded and grown in a green house for 40 days. Each of the compounds of the present invention 1 to 4, 9 to 11, 16 to 19, 21, 23, 34 to 36, 40, 41, 45, 46, 49, 50, 55, 61, 63, 68, 70 to 73, 77 to 79, 81, 83, 84, 86 to 92, 95 to 97, 102, 103, 105 to 112, 116 and 120 to 129 was formulated according to Formulation Example 6, then, diluted with water to provide prescribed concentration(200ppm), and these diluted solutions were sprayed onto stems and leaves so as to give sufficient adhesion on the surface of grape leaves. After spraying, the liquid on the stem was air-dried, and a suspension of zoosporangia of *Plasmopara viticola* (about 10,000 zoosporangia were contained in 1ml of the suspension) was inoculated by spraying(the amount of the sprayed suspension was about 2 ml for one plant). After inoculation, the plant was first grown for one day at 23°C under 90 % or more humidity, then further grown for 6 days in the green house, which was 24°C in daytime and 20°C in night-time. Then, the areas of a lesion of the plants were observed.

As a result, the lesion areas on the plants treated with the compounds of the present invention 1 to 4, 9 to 11, 16 to 19, 21, 23, 34 to 36, 40, 41, 45, 46, 49, 50, 55, 61, 63, 68, 70 to 73, 77 to 79, 81, 83, 84, 86 to 92, 95 to 97, 102, 103, 105 to 112, 116 and 120 to 129 were not more than 10% of the lesion area on a non-treatment plant.

#### Test Example 4

Sand loam was compacted in a plastic pot, and a grape (variety: Berry A) was seeded and grown in a green house for 40 days. Each of the compounds of the present invention 6, 13



to 15, 20, 27 to 33, 37 to 39, 48, 53, 54, 62, 64, 66, 67, 69, 74 to 76, 93, 98 to 100, 115 and 118 was formulated according to Formulation Example 6, then, diluted with water to provide prescribed concentration(50ppm), and these diluted solutions  
5 were sprayed onto stems and leaves so as to give sufficient adhesion on the surface of grape leaves. After spraying, the liquid on the stem was air-dried, and a suspension of zoospores of *Plasmopara viticola* (about 10,000 zoospores were contained in 1ml of the suspension) was inoculated by spraying (the amount  
10 of the sprayed suspension was about 2 ml for one plant). After inoculation, the plant was first grown for one day at 23°C under 90 % or more humidity, then further grown for 6 days in the green house, which was 24°C in daytime and 20°C in night-time. Then, the areas of a lesion of the plants were observed.

15 As a result, the lesion areas on the plants treated with the compounds of the present invention 6, 13 to 15, 20, 27 to 33, 37 to 39, 48, 53, 54, 62, 64, 66, 67, 69, 74 to 76, 93, 98 to 100, 115 and 118 were not more than 10% of the lesion area on a non-treatment plant.

#### 20 Test Example 5

Sand loam was compacted in a plastic pot, and a grape (variety: Berry A) was seeded and grown in a green house for 40 days. Each of the compounds of the present invention 5, 7, 8, 12, 44, 56, 59 and 85 was formulated according to Formulation  
25 Example 6, then, diluted with water to provide prescribed concentration(12.5ppm), and these diluted solutions were sprayed onto stems and leaves so as to give sufficient adhesion on the surface of grape leaves. After spraying, the liquid on the stem

was air-dried, and a suspension of zoosporangia of *Plasmopara viticola* (about 10,000 zoosporangia were contained in 1ml of the suspension) was inoculated by spraying (the amount of the sprayed suspension was about 2 ml for one plant). After  
5 inoculation, the plant was first grown for one day at 23°C under 90 % or more humidity, then further grown for 6 days in the green house, which was 24°C in daytime and 20°C in night-time. Then, the areas of a lesion of the plants were observed.

As a result, the lesion areas on the plants treated with  
10 the compounds of the present invention 5, 7, 8, 12, 44, 56, 59 and 85 were not more than 10% of the lesion area on a non-treatment plant.

#### Industrial Applicability

15 Plant diseases can be controlled by using the compound of the present compounds.